

# EXHIBIT 14

B234739

**THE UNITED STATES OF AMERICA****TO ALL TO WHOM THESE PRESENTS SHALL COME:****UNITED STATES DEPARTMENT OF COMMERCE****United States Patent and Trademark Office**

April 25, 2022

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE  
RECORDS OF THIS OFFICE OF THE FILE WRAPPER AND CONTENTS  
OF:

APPLICATION NUMBER: 15/705,172

FILING DATE: September 14, 2017

PATENT NUMBER: 9,994,851

ISSUE DATE: June 12, 2018

By Authority of the  
Under Secretary of Commerce for Intellectual Property  
and Director of the United States Patent and Trademark Office



*W. Montgomery*  
Wanda Montgomery  
Certifying Officer

Doc Code: TRACK1.REQ

Document Description: TrackOne Request

PTO/AIA/424 (04-14)

<b>CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION</b> <b>UNDER 37 CFR 1.102(e) (Page 1 of 1)</b>			
First Named Inventor:	Stephen Donald WILTON	Nonprovisional Application Number (if known):	Not Yet Assigned
Title of Invention:	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		
<p><b>APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.</b></p> <ol style="list-style-type: none"> <li>1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently \$0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.</li> <li>2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.</li> <li>3. The applicable box is checked below:               <div style="margin-left: 20px;"> <p><b>I. <input checked="checked" type="checkbox"/> <u>Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)</u></b></p> <ol style="list-style-type: none"> <li>i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web. ---OR---</li> <li>(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.</li> <li>ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, <u>or</u> the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.</li> </ol> <p><b>II. <input type="checkbox"/> <u>Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)</u></b></p> <ol style="list-style-type: none"> <li>i. A request for continued examination has been filed with, or prior to, this form.</li> <li>ii. If the application is a utility application, this certification and request is being filed via EFS-Web.</li> <li>iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.</li> <li>iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.</li> <li>v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).</li> </ol> </div> </li> </ol>			
Signature /Amy E. Mandragouras, Esq./		Date September 14, 2017	
Name (Print/Typed) Amy E. Mandragouras, Esq.		Practitioner Registration Number 36,207	
<p><b>Note:</b> This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*</p>			
<div style="border: 1px solid black; padding: 5px;"> <input type="checkbox"/> *Total of <u>1</u> forms are submitted.         </div>			
<p>I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).</p> <p>Dated: September 14, 2017 <span style="float: right;">Electronic Signature for Amy E. Mandragouras, Esq.: /Amy E. Mandragouras, Esq./</span></p>			

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 14, 2017  
Electronic Signature for Amy E. Mandragouras, Esq.:/ Amy E. Mandragouras, Esq./

Docket No.: AVN-008CN41  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Stephen Donald Wilton *et al.*

Application No.: Not Yet Assigned

Confirmation No.: N/A

Filed: Concurrently Herewith

Art Unit: N/A

For: ANTISENSE OLIGONUCLEOTIDES FOR  
INDUCING EXON SKIPPING AND  
METHODS OF USE THEREOF

Examiner: Not Yet Assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**STATEMENT PURSUANT TO 37 CFR 1.821**

Dear Sir:

Submitted herewith in connection with the above-referenced patent application and in full compliance with 37 C.F.R. §§1.821-1.825 is a computer readable copy and paper copy of the Sequence Listing (filed together as a .txt file via the United States Patent Office's Electronic Filing System).

I hereby state that I have reviewed the paper copy of the Sequence Listing, as required by 37 CFR 1.821(c), and have reviewed the computer readable form of the Sequence Listing, as required by 37 CFR 1.821(e), and that the content of the paper and computer readable copies for the above-referenced patent application are the same as required by 37 CFR 1.821(f) (note that these documents are submitted as one electronic file). No new matter has been added to the Sequence Listing.



Application No.: Not Yet Assigned

Docket No.: AVN-008CN41

Dated: September 14, 2017

Respectfully submitted,

Electronic signature: /Amy E. Mandragouras,  
Esq./  
Amy E. Mandragouras, Esq.  
Registration No.: 36,207  
NELSON MULLINS RILEY & SCARBOROUGH LLP  
One Post Office Square  
Boston, Massachusetts 02109-2127  
(617) 217-4626  
(617) 217-4699 (Fax)  
Attorney/Agent For Applicant

PTO/AIA/01 (06-12)

Approved for use through 01/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN  
APPLICATION DATA SHEET (37 CFR 1.76)****Title of  
Invention****ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING  
AND METHODS OF USE THEREOF**

As the below named inventor, I hereby declare that:

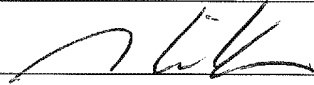
This declaration ☐ The attached application, or  
is directed to:☒ United States application or PCT international application number 13/741,150  
filed on 01/14/2013

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001  
by fine or imprisonment of not more than five (5) years, or both.**WARNING:**

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

**LEGAL NAME OF INVENTOR**Inventor: Stephen Donald WILTONDate (Optional): 26/03/13Signature: 

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

PTO/AIA/01 (06-12)

Approved for use through 01/31/2014. OMB 0651-0032

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This declaration ☐ The attached application, or  
is directed to:☒ United States application or PCT international application number 13/741,150  
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**LEGAL NAME OF INVENTOR**Inventor: Sue FLETCHERDate (Optional): 26/03/2013Signature: 

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

PTO/AIA/01 (06-12)

Approved for use through 01/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN  
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Invention****ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING  
AND METHODS OF USE THEREOF**

As the below named inventor, I hereby declare that:

This declaration ☐ The attached application, or  
is directed to:☒ United States application or PCT international application number 13/741,150  
filed on 01/14/2013

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

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by fine or imprisonment of not more than five (5) years, or both.**WARNING:**

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**LEGAL NAME OF INVENTOR**Inventor: Graham MCCLOREYDate (Optional): 26-03-13Signature: *Graham McClorey*

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

## Secrecy Order 37 CFR 5.2:

<input type="checkbox"/>	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
--------------------------	---

## Inventor Information:

Inventor	1				<a href="#">Remove</a>	
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Stephen	Donald	WILTON			
Residence Information (Select One)    US Residency <input checked="" type="radio"/> Non US Residency    Active US Military Service						
City	Applecross		Country of Residence <sup>i</sup>	AU		
Mailing Address of Inventor:						
Address 1		18 Spey Road				
Address 2						
City	Applecross		State/Province			
Postal Code	6153		Country <sup>i</sup>	AU		
Inventor	2				<a href="#">Remove</a>	
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Sue		FLETCHER			
Residence Information (Select One)    US Residency <input checked="" type="radio"/> Non US Residency    Active US Military Service						
City	Bayswater		Country of Residence <sup>i</sup>	AU		
Mailing Address of Inventor:						
Address 1		14 Roberts Street				
Address 2						
City	Bayswater		State/Province			
Postal Code	6053		Country <sup>i</sup>	AU		
Inventor	3				<a href="#">Remove</a>	
Legal Name						



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

Prefix	Given Name	Middle Name	Family Name	Suffix
	Graham		McCLOREY	
<b>Residence Information (Select One)</b>		US Residency <input type="radio"/> Non US Residency <input checked="" type="radio"/> Active US Military Service <input type="checkbox"/>		
City	Bayswater	Country of Residence <sup>i</sup>	AU	

#### Mailing Address of Inventor:

Address 1	8 Digwood Close			
Address 2				
City	Bayswater	State/Province		
Postal Code	6053	Country <sup>i</sup>	AU	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the <b>Add</b> button. <div style="float: right; border: 1px solid black; padding: 2px 5px;">Add</div>				

#### Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).			
<input type="checkbox"/> An Address is being provided for the correspondence Information of this application.			
Customer Number	123147		
Email Address	ipboston.docketing@nelsonmullins.com	<div>Add Email</div>	<div>Remove Email</div>

#### Application Information:

Title of the Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		
Attorney Docket Number	AVN-008CN41	Small Entity Status Claimed <input checked="" type="checkbox"/>	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	22	Suggested Figure for Publication (if any)	

#### Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country <sup>i</sup>

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

### Publication Information:

<input type="checkbox"/> Request Early Publication (Fee required at time of Request 37 CFR 1.219)
<input type="checkbox"/> <b>Request Not to Publish.</b> I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application <b>has not and will not</b> be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

### Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.			
Please Select One:	<input checked="" type="radio"/> Customer Number	<input type="radio"/> US Patent Practitioner	<input type="radio"/> Limited Recognition (37 CFR 11.9)
Customer Number	123147		

### Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78. When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove		
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
	Continuation of	15/274772	2017-09-23		
Prior Application Status	Patented		Remove		
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15/274772	Continuation of	14/740097	2015-06-15	9605262B	2017-03-28
Prior Application Status	Abandoned		Remove		
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
14/740097	Continuation of	13/741150	2013-01-14		
Prior Application Status	Abandoned		Remove		
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
13/741150	Continuation of	13/168857	2011-06-24		

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number		AVN-008CN41	
		Application Number			
Title of Invention		ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF			

Prior Application Status		Patented		Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
13/168857	Continuation of	12/837359	2010-07-15	8232384B	2012-07-31
Prior Application Status		Patented		Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
12/837359	Continuation of	11/570691	2008-01-15	7807816B	2010-10-05
Prior Application Status				Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
11/570691	a 371 of international	PCT/AU2005/000943	2005-06-28		
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the <b>Add</b> button.					

## Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)<sup>i</sup> the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Application Number		Country <sup>i</sup>	Filing Date (YYYY-MM-DD)	Access Code <sup>j</sup> (if applicable)	Remove
2004903474		AU	2004-06-28		
Additional Foreign Priority Data may be generated within this form by selecting the <b>Add</b> button.					Add

## Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

- ☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
- NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

## Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

**NOTE:** This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

### 1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

**A. Priority Document Exchange (PDX)** - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

**B. Search Results from U.S. Application to EPO** - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

### 2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

**NOTE:** Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
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Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

## Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

<b>Applicant</b>	1	<input type="button" value="Remove"/>
<p>If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.</p>		
<input type="button" value="Clear"/>		
<input checked="" type="radio"/> Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.		Person who shows sufficient proprietary interest
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:		
<div style="border: 1px solid black; height: 20px; width: 100%;"></div>		
Name of the Deceased or Legally Incapacitated Inventor: <div style="border: 1px solid black; height: 20px; width: 100%;"></div>		
If the Applicant is an Organization check here. <input checked="" type="checkbox"/>		
Organization Name	The University of Western Australia	
<b>Mailing Address Information For Applicant:</b>		
Address 1	35 Stirling Highway	
Address 2		
City	Crawley	State/Province
Country	AU	Postal Code
Phone Number		Fax Number
Email Address		
Additional Applicant Data may be generated within this form by selecting the Add button. <input type="button" value="Add"/>		

## Assignee Information including Non-Applicant Assignee Information:

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

<b>Assignee</b>	1			
Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.				
				<a href="#">Remove</a>
If the Assignee or Non-Applicant Assignee is an Organization check here.				<input type="checkbox"/>
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<b>Mailing Address Information For Assignee including Non-Applicant Assignee:</b>				
Address 1				
Address 2				
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**NOTE:** This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

<b>Signature</b>	/Amy E. Mandragouras, Esq./		Date (YYYY-MM-DD)	2017-09-14
First Name	Amy	Last Name	Mandragouras	Registration Number
			36,207	
Additional Signature may be generated within this form by selecting the Add button.				<a href="#">Add</a>

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	AVN-008CN41
		Application Number	
Title of Invention	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

FIGURE 1

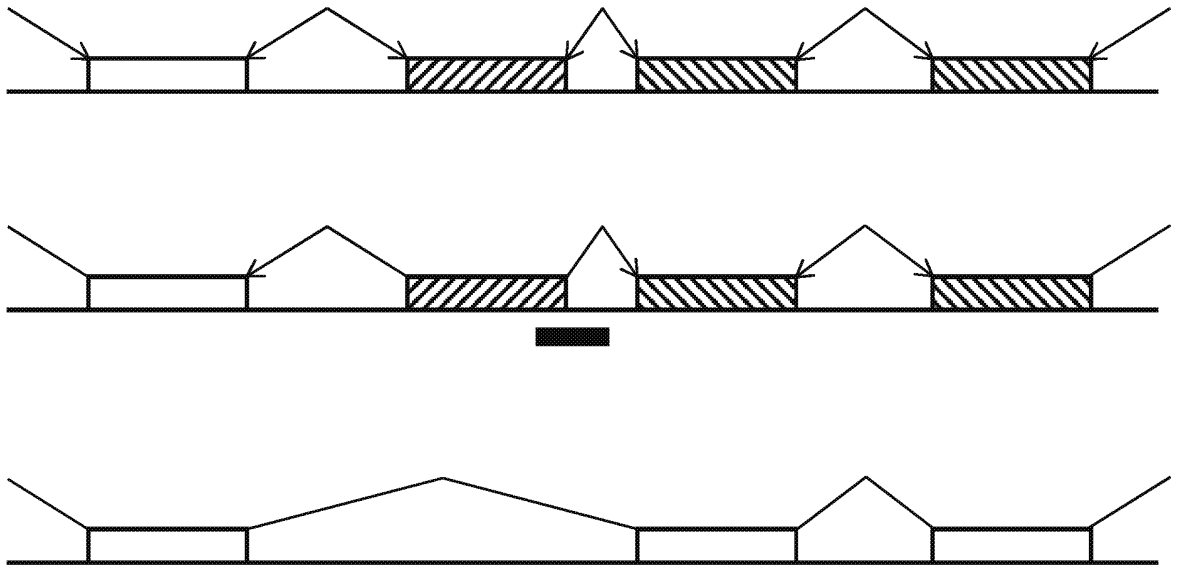
1/22

bp	Acceptor	ESE	Donor
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3	u	g	c
4	c	a	c
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6	g	u	g
7	u	g	a
8	g	a	c
9	a	g	a
10	g	a	c
11	c	a	u
12	c	u	g
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100	u	g	a

SEQ ID NO:213

SEQ ID NO:214

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**FIGURE 2**



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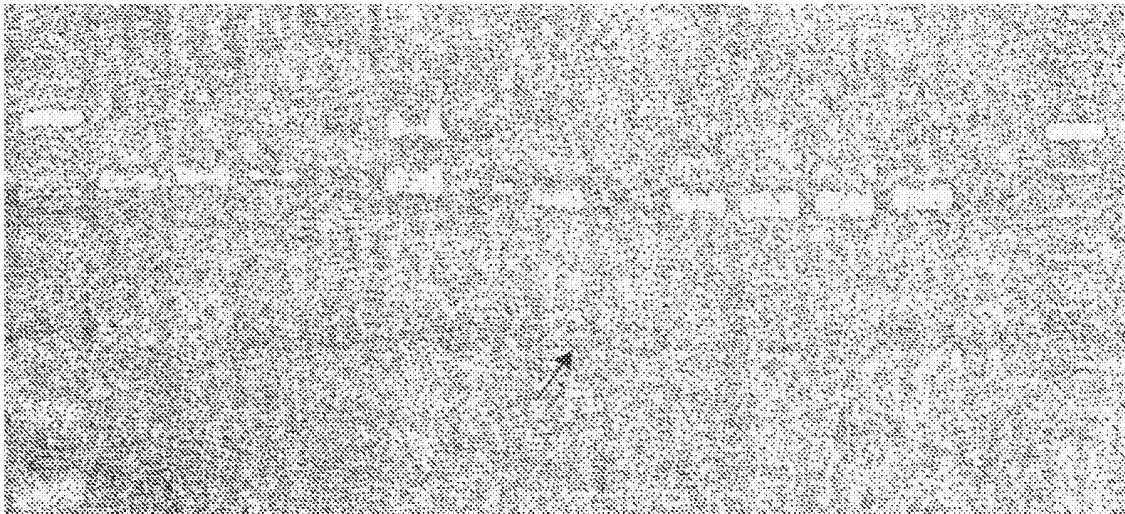
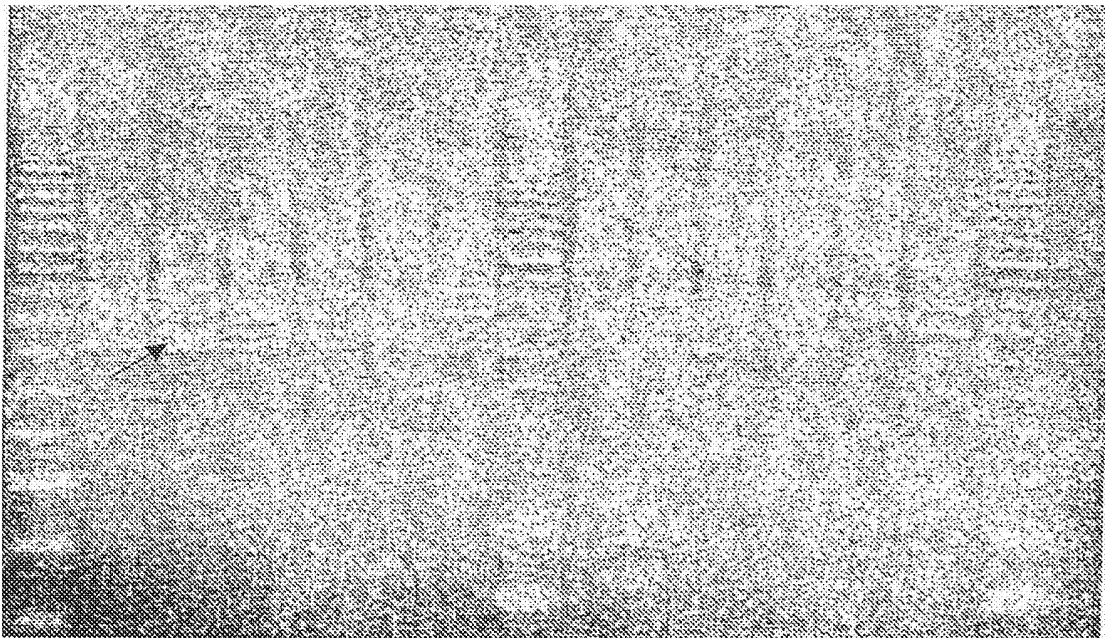


FIGURE 3

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H7A(+45+67) H7A(+2+26)  
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**FIGURE 4**

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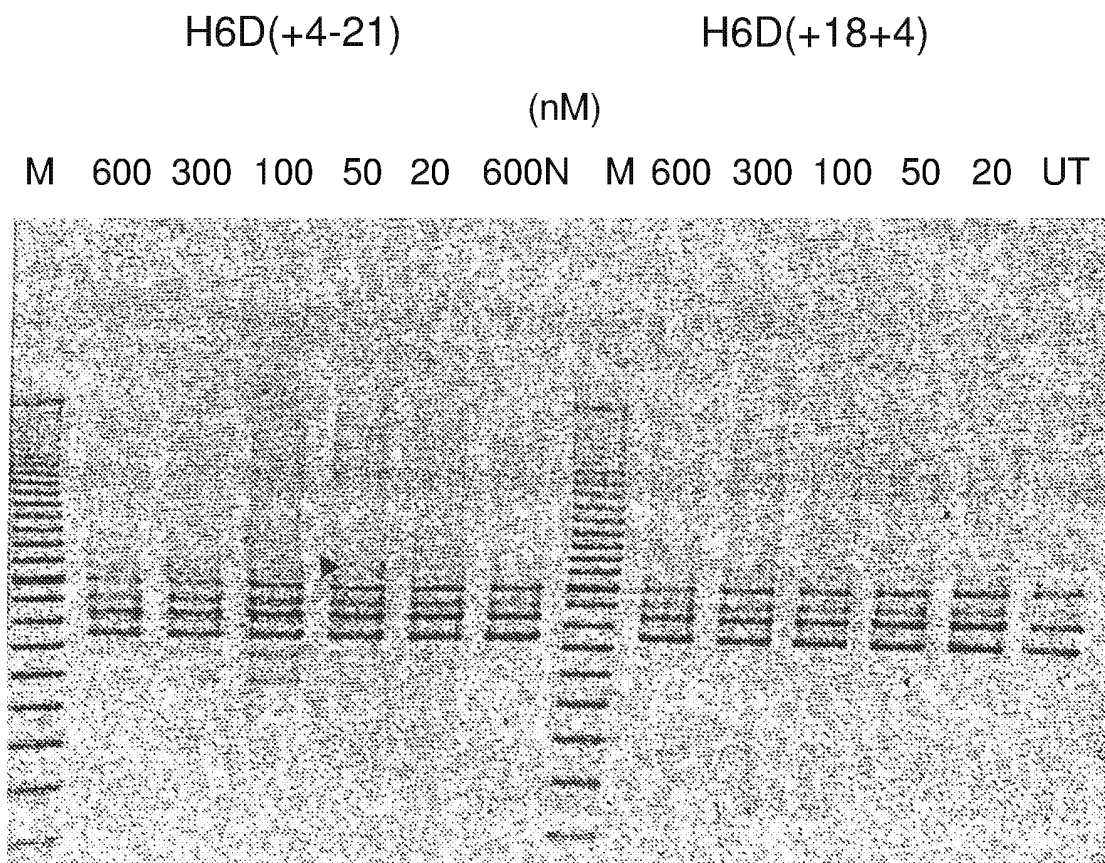
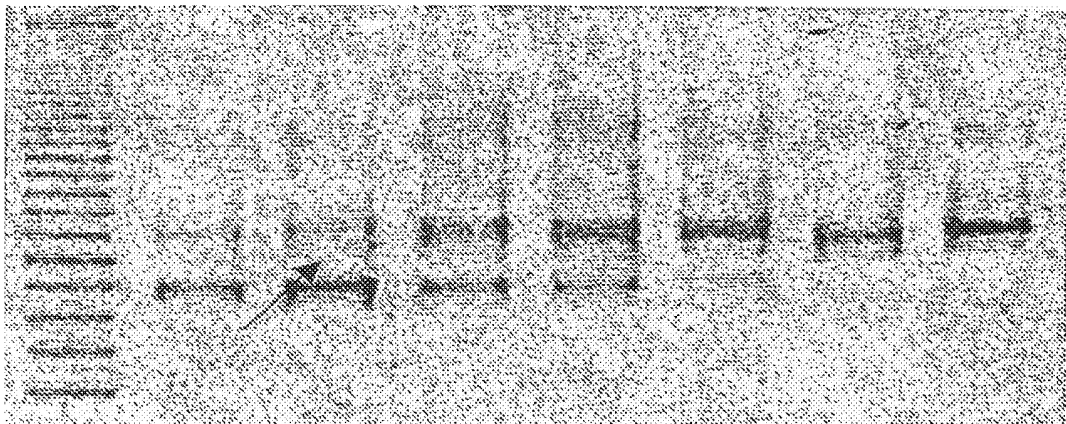


FIGURE 5

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6A(+69+91)

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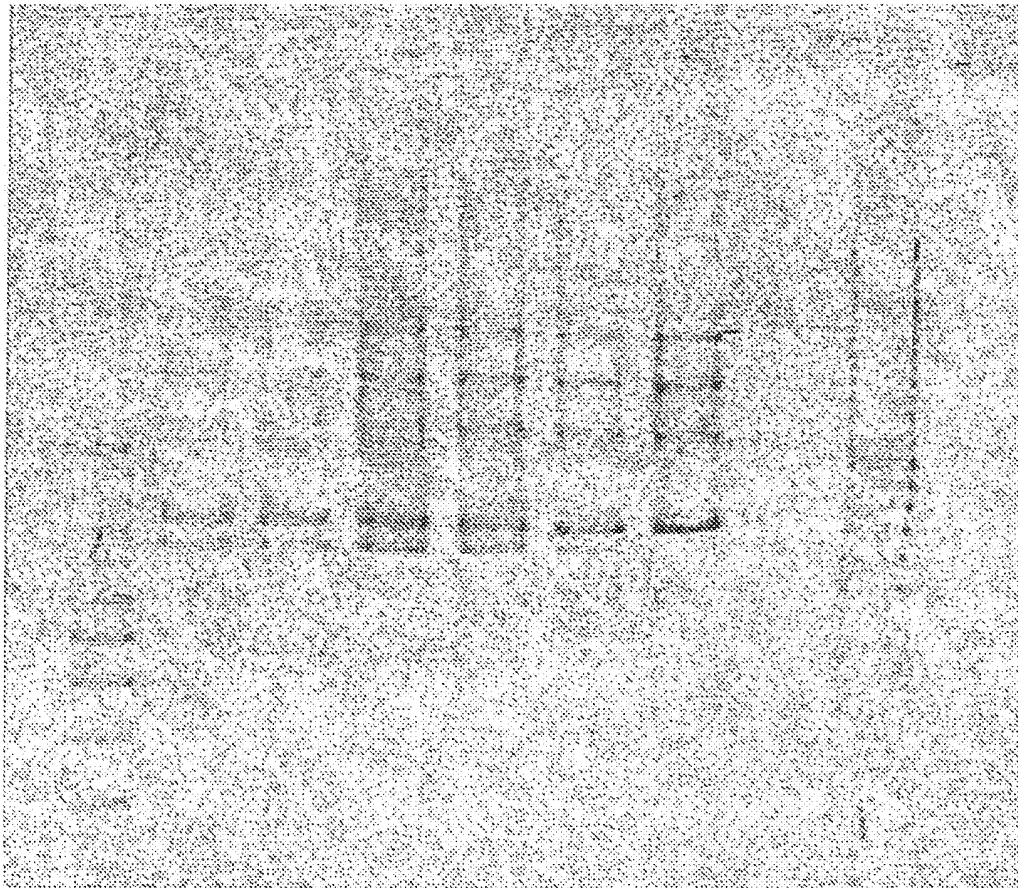
**FIGURE 6**



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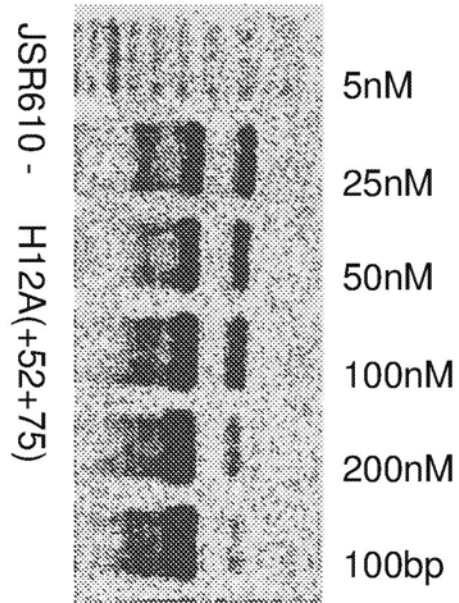
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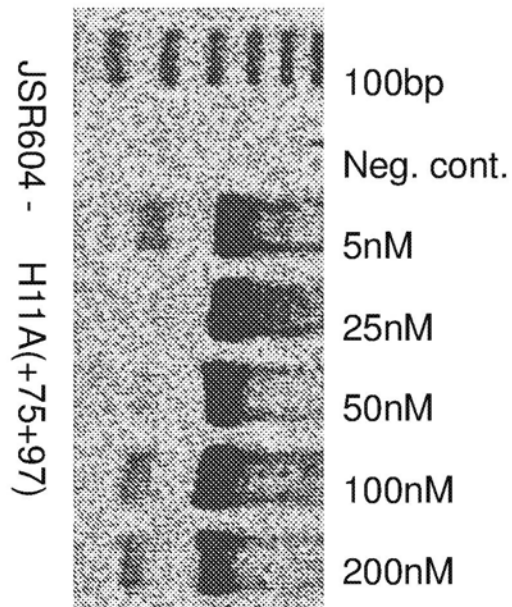


**FIGURE 7**

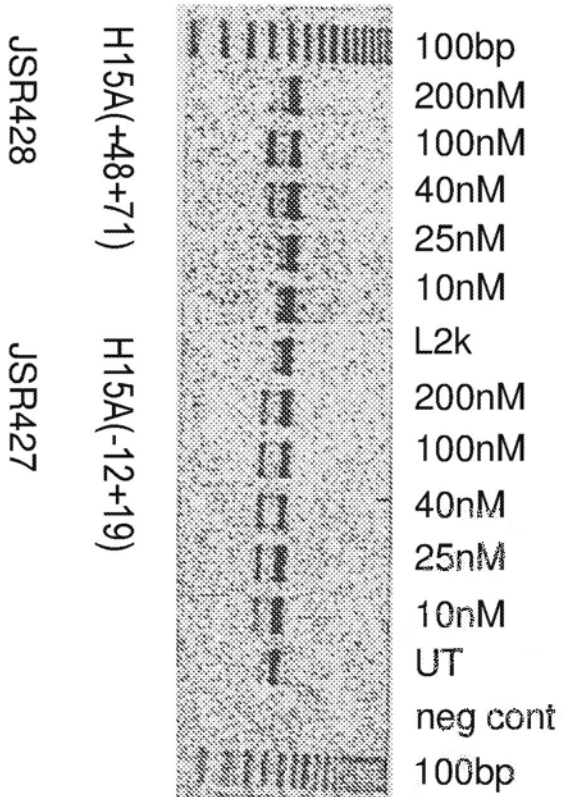




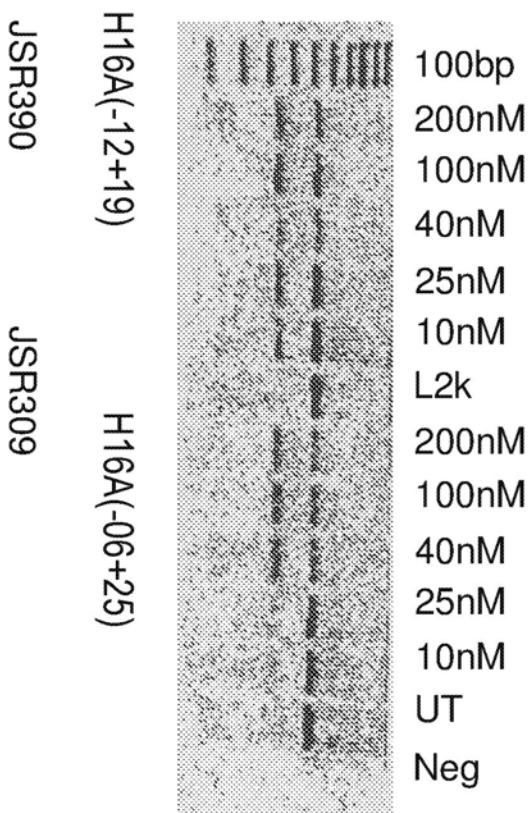
**FIGURE 8A**



**FIGURE 8B**

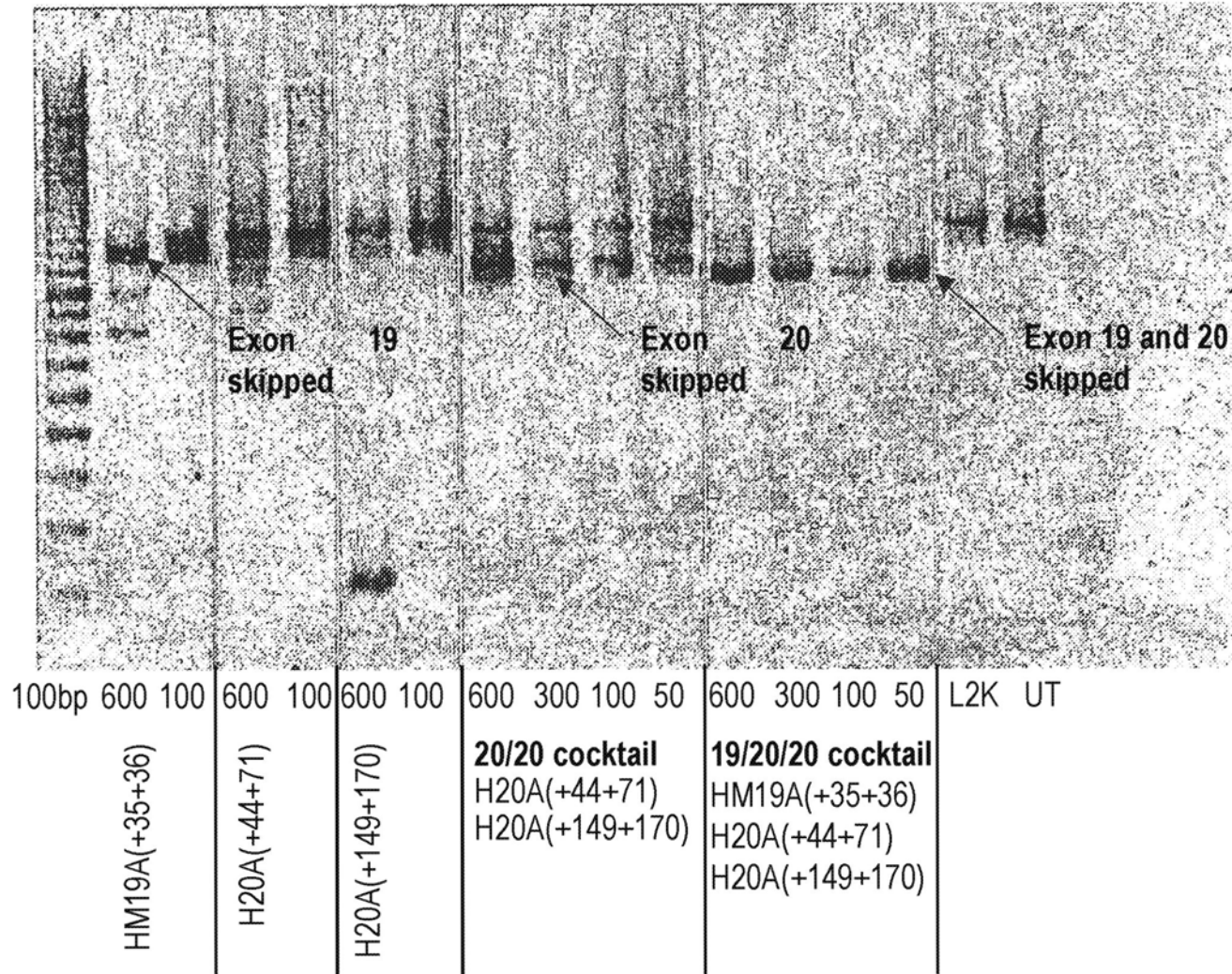


**FIGURE 9A**



**FIGURE 9B**

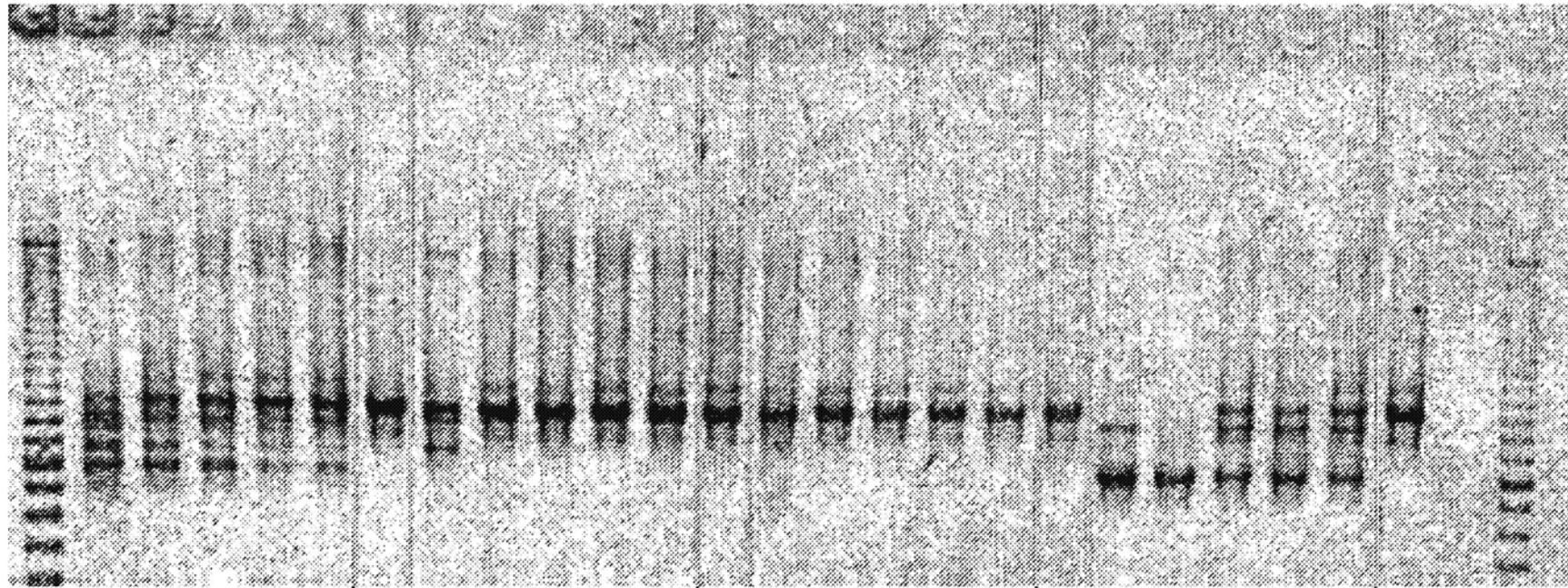




**FIGURE 10**

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H20A(+44+63)-aa-  
H20A(+149+168)

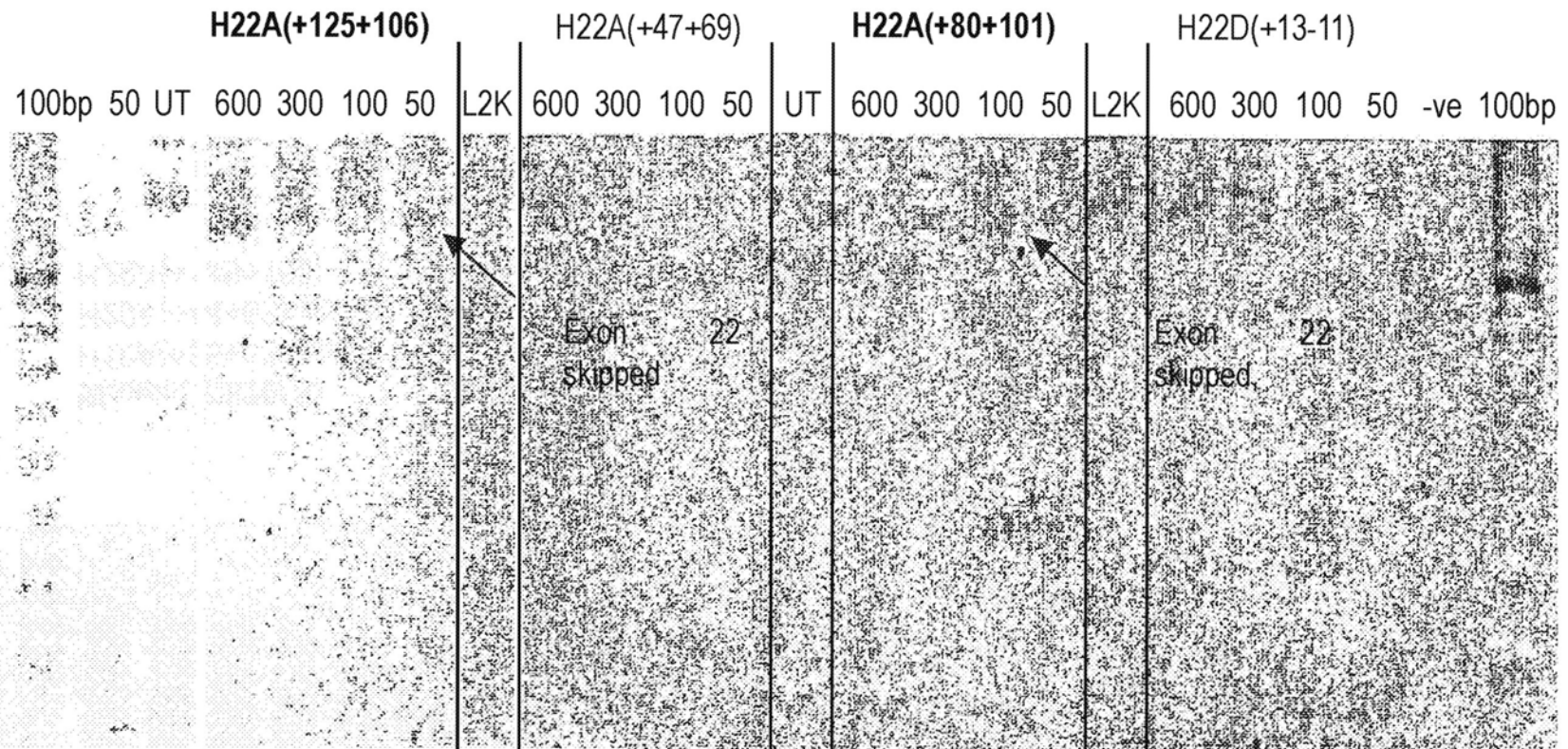
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aa-  
H20A(+44+63)

**Weasel19/20**  
H19A(+35+53)-  
aa-  
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**19/20/20 cocktail**  
HM19A(+35+36)  
H20A(+44+71)  
H20A(+149+170)

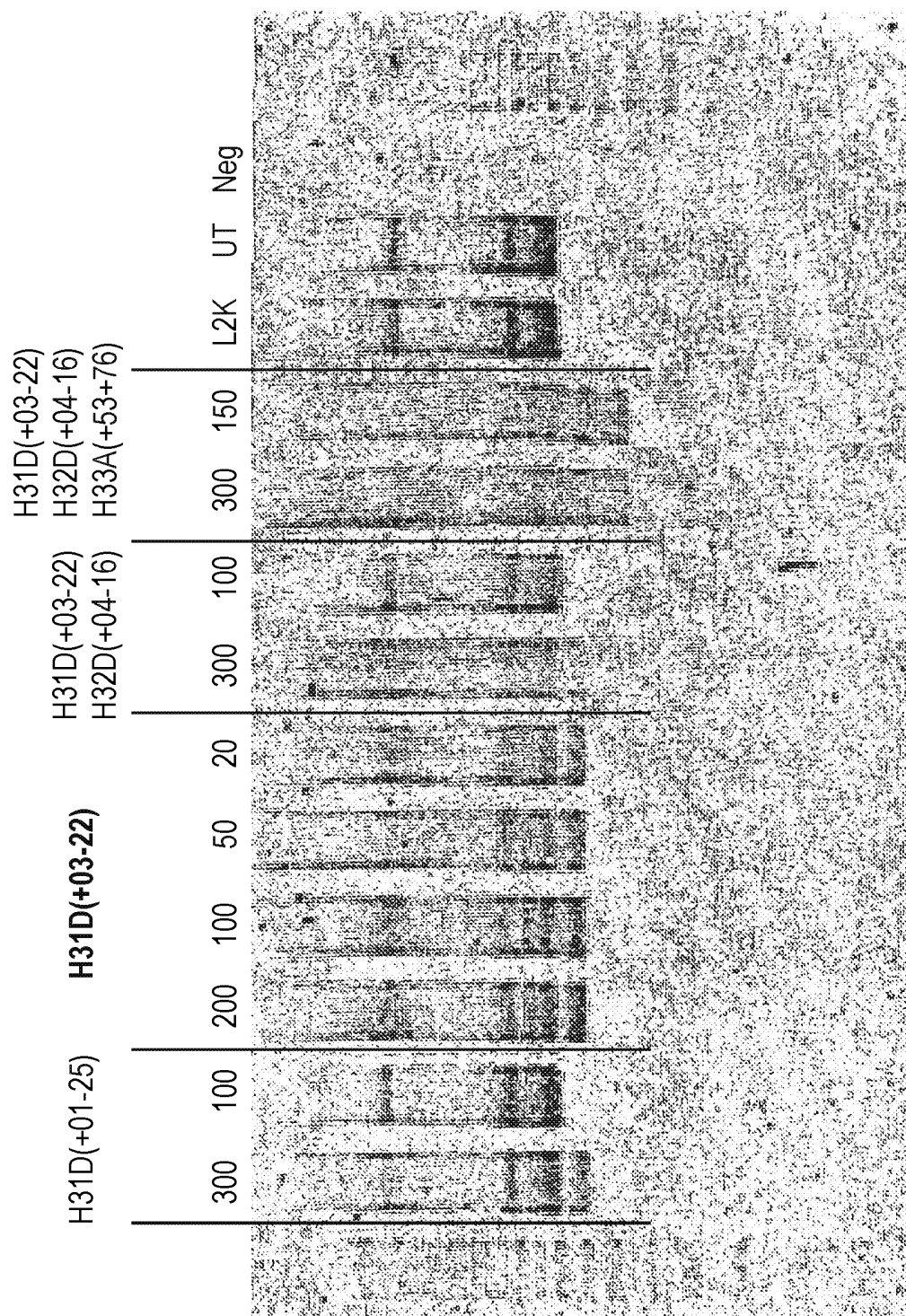
**FIGURE 11**





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FIGURE 12





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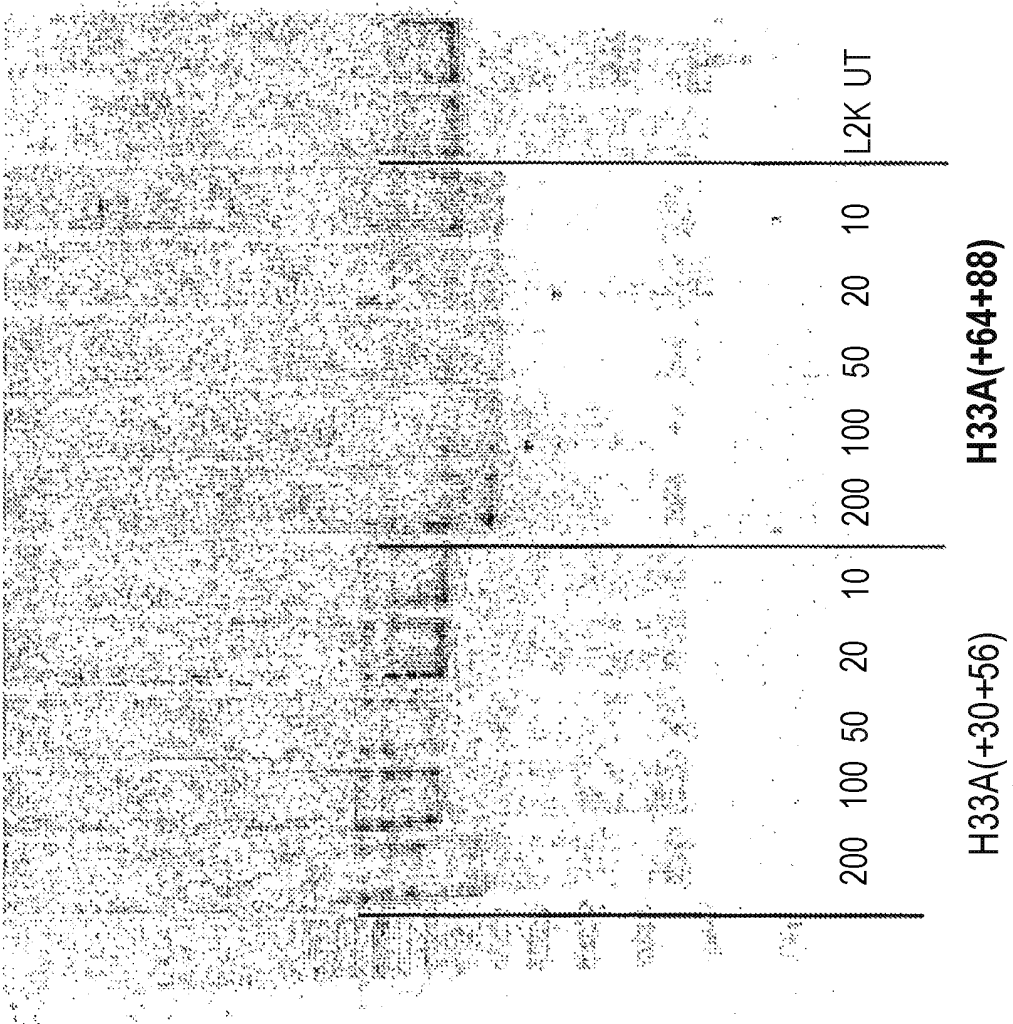


FIGURE 14

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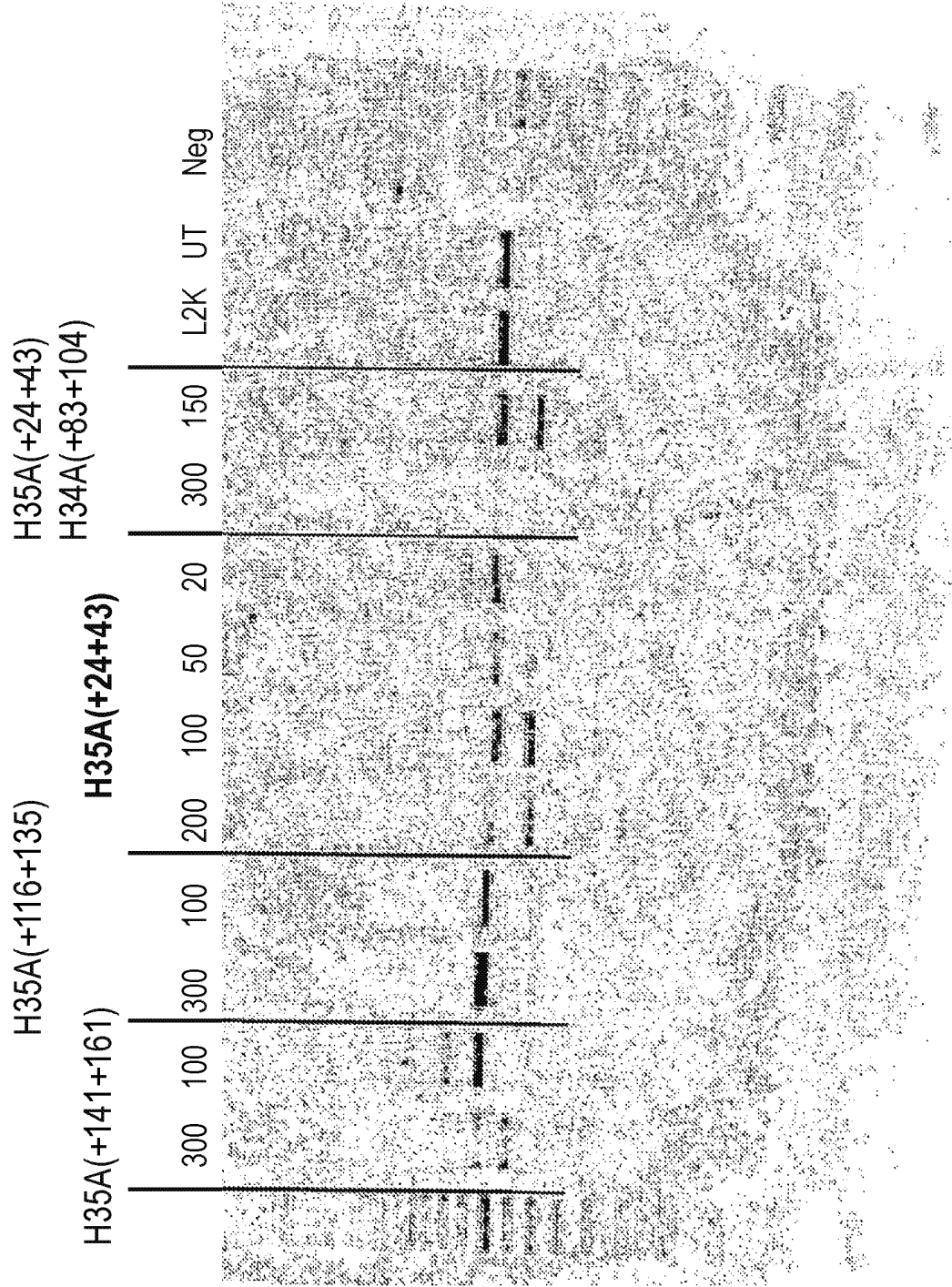
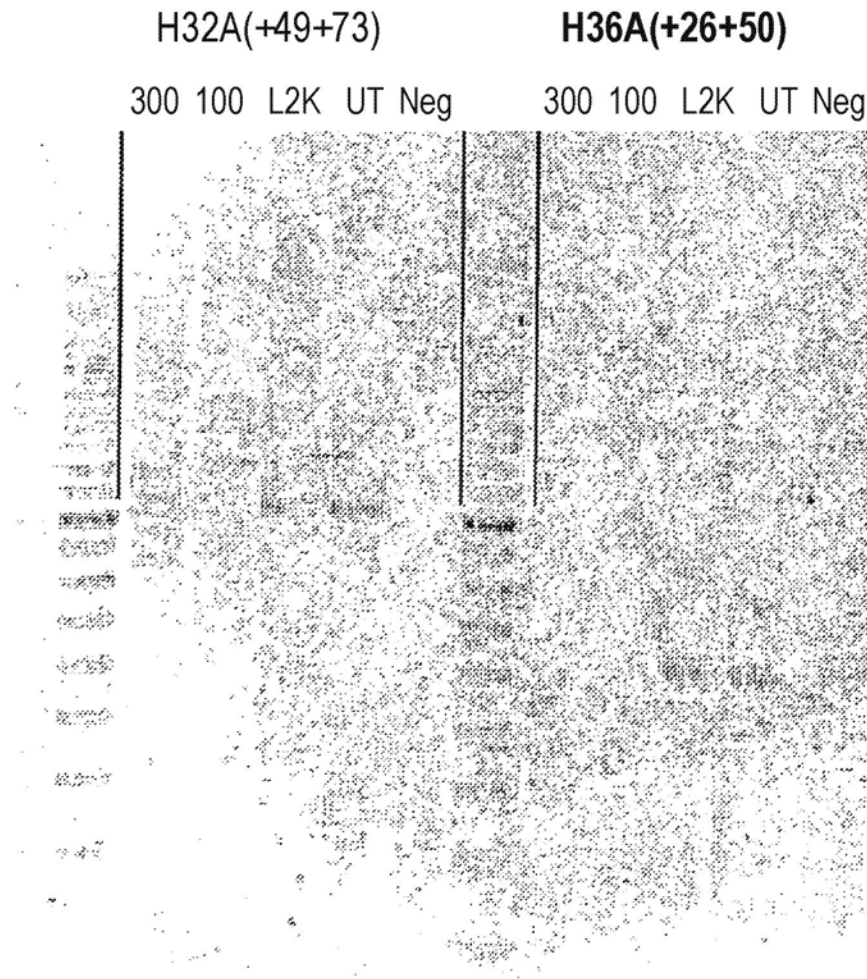


FIGURE 15





**FIGURE 16**

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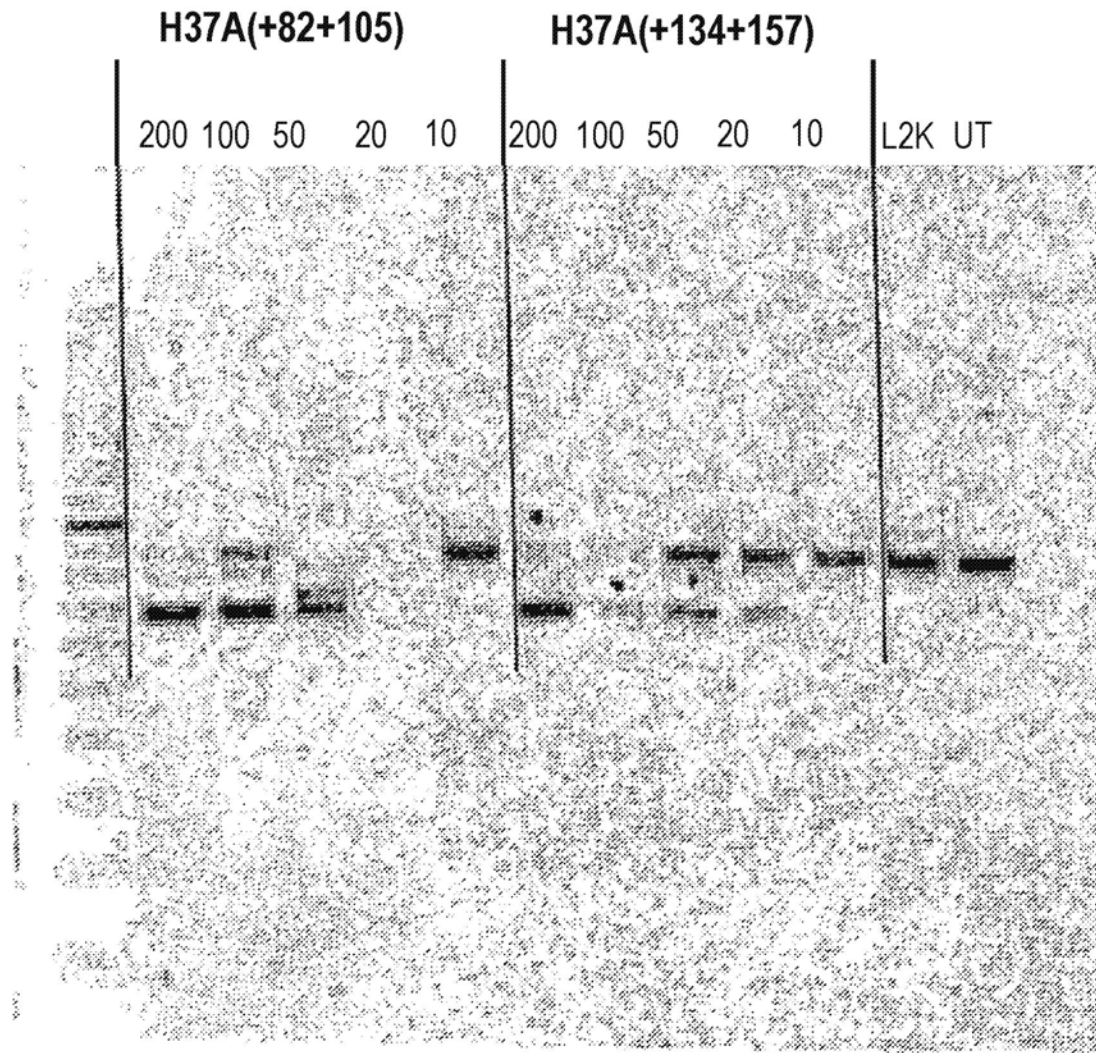
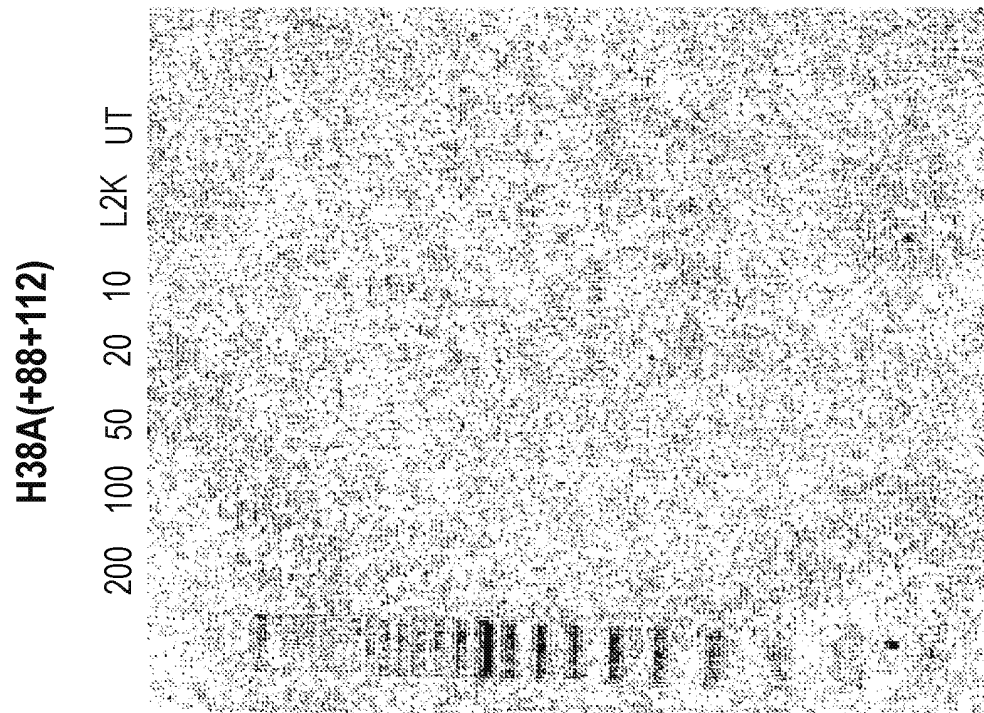


FIGURE 17

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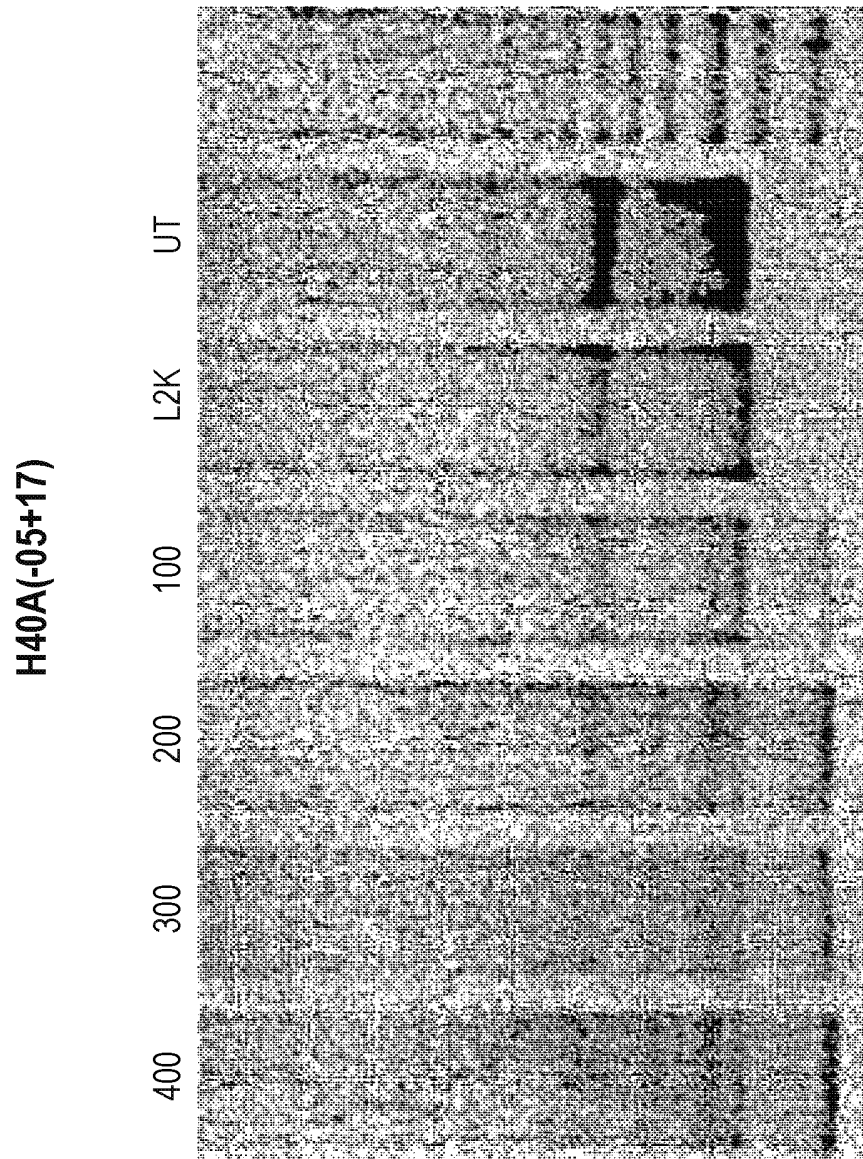
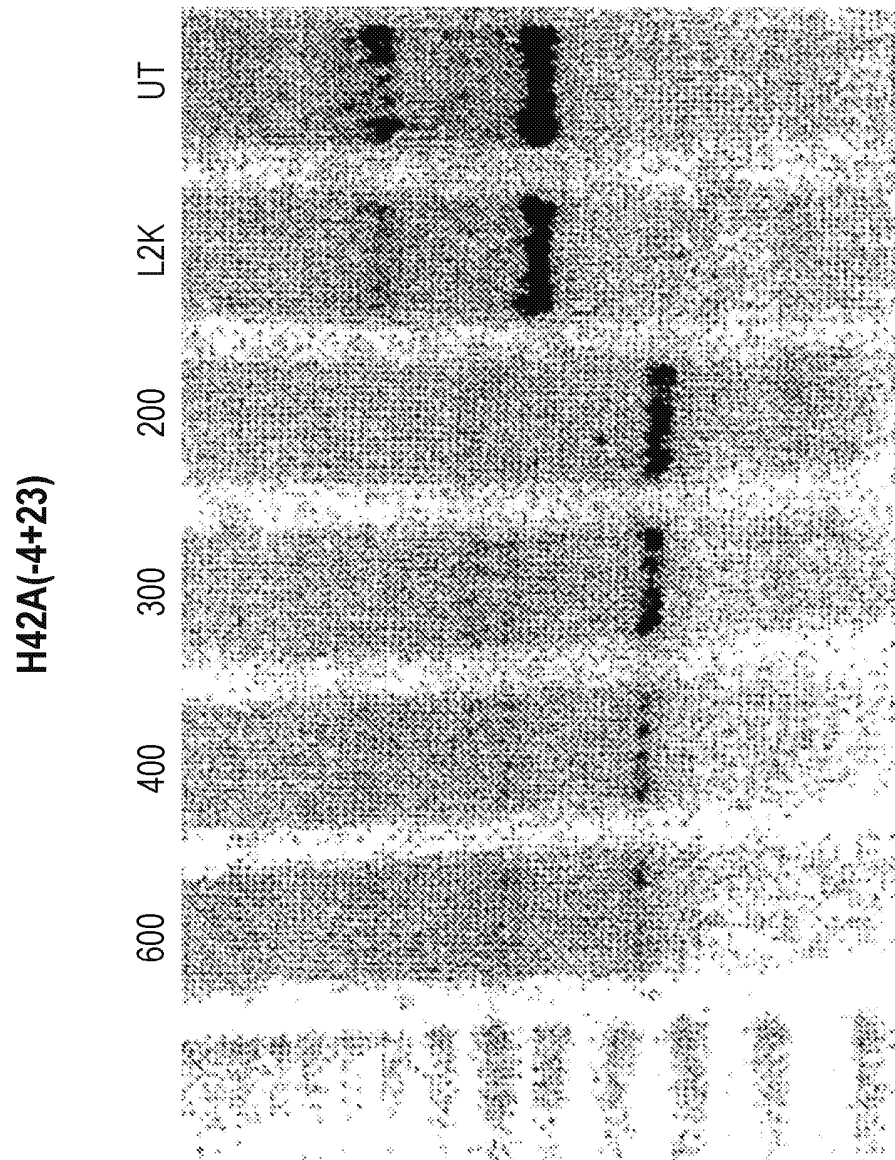


FIGURE 19

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**FIGURE 20**

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H46A(+86+115)

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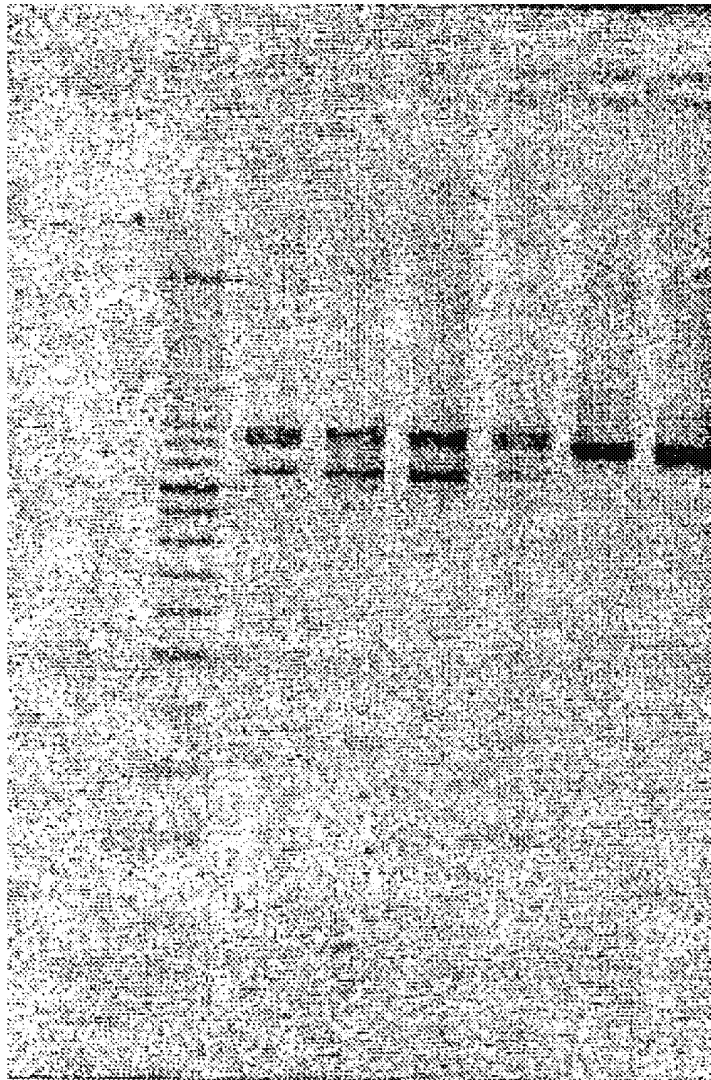
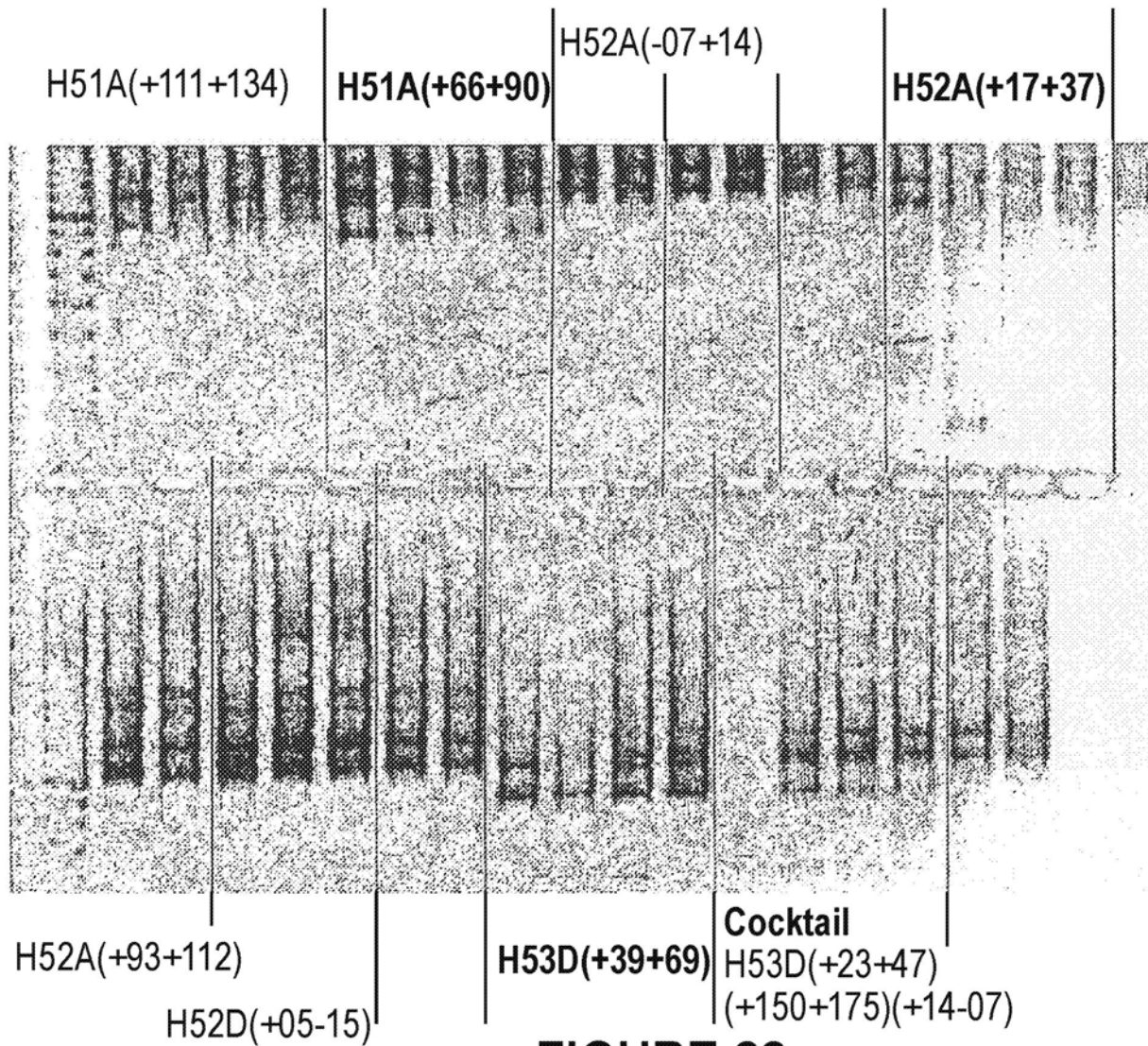


FIGURE 21





**FIGURE 22**

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ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING  
AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

5                   This application is a continuation of U.S. Patent Application No. 15/274,772, filed September 23, 2016, now pending, which application is a continuation of U.S. Patent Application No 14/740,097, filed June 15, 2015, now issued as U.S. Patent No. 9,605,262, which application is a continuation of U.S. Patent Application No. 13/741,150, filed January 14, 2013, now abandoned, which application is a continuation of U.S. Patent  
10   Application No. 13/168,857, filed June 24, 2011, now abandoned, which application is a continuation of U.S. Patent Application No. 12/837,359, filed July 15, 2010, now issued as U.S. Patent No. 8,232,384, which application is a continuation of U.S. Patent Application No. 11/570,691, filed January 15, 2008, now issued as U.S. Patent No. 7,807,816, which application is a 35 U.S.C. § 371 National Phase Application of PCT/AU2005/000943, filed  
15   June 28, 2005, which claims priority to Australian Patent Application No. 2004903474, filed June 28, 2004; which applications are each incorporated herein by reference in their entireties.

STATEMENT REGARDING SEQUENCE LISTING

20                   The Sequence Listing associated with the application is provided in text format in lieu of a paper copy, and is hereby incorporated by reference into the specification. The name of the text file containing the Sequence Listing is AVN-008CN41\_Sequence-Listing.txt. The text file is 62,086 Kilobytes, was created on September 14, 2017 and is being submitted electronically via EFS-Web.

25   FIELD OF THE INVENTION

                  The present invention relates to novel antisense compounds and compositions suitable for facilitating exon skipping. It also provides methods for inducing



exon skipping using the novel antisense compounds as well as therapeutic compositions adapted for use in the methods of the invention.

## BACKGROUND ART

5 Significant effort is currently being expended researching methods for suppressing or compensating for disease-causing mutations in genes. Antisense technologies are being developed using a range of chemistries to affect gene expression at a variety of different levels (transcription, splicing, stability, translation). Much of that research has focused on the use of antisense compounds to correct or compensate for abnormal or disease-associated genes in a myriad of different conditions.

10 Antisense molecules are able to inhibit gene expression with exquisite specificity and because of this many research efforts concerning oligonucleotides as modulators of gene expression have focused on inhibiting the expression of targeted genes such as oncogenes or viral genes. The antisense oligonucleotides are directed either against RNA (sense strand) or against DNA where they form triplex structures inhibiting  
15 transcription by RNA polymerase II. To achieve a desired effect in specific gene down-regulation, the oligonucleotides must either promote the decay of the targeted mRNA or block translation of that mRNA, thereby effectively preventing *de novo* synthesis of the undesirable target protein.

Such techniques are not useful where the object is to up-regulate production  
20 of the native protein or compensate for mutations which induce premature termination of translation such as nonsense or frame-shifting mutations. Furthermore, in cases where a normally functional protein is prematurely terminated because of mutations therein, a means for restoring some functional protein production through antisense technology has been shown to be possible through intervention during the splicing processes (Sierakowska  
25 H, *et al.*, (1996) Proc Natl Acad Sci USA 93, 12840-12844; Wilton SD, *et al.*, (1999) Neuromusc Disorders 9, 330-338; van Deutekom JC *et al.*, (2001) Human Mol Genet 10, 1547-1554). In these cases, the defective gene transcript should not be subjected to

targeted degradation so the antisense oligonucleotide chemistry should not promote target mRNA decay.

In a variety of genetic diseases, the effects of mutations on the eventual expression of a gene can be modulated through a process of targeted exon skipping during the splicing process. The splicing process is directed by complex multi-particle machinery that brings adjacent exon-intron junctions in pre-mRNA into close proximity and performs cleavage of phosphodiester bonds at the ends of the introns with their subsequent reformation between exons that are to be spliced together. This complex and highly precise process is mediated by sequence motifs in the pre-mRNA that are relatively short semi-conserved RNA segments to which bind the various nuclear splicing factors that are then involved in the splicing reactions. By changing the way the splicing machinery reads or recognises the motifs involved in pre-mRNA processing, it is possible to create differentially spliced mRNA molecules. It has now been recognised that the majority of human genes are alternatively spliced during normal gene expression, although the mechanisms invoked have not been identified. Using antisense oligonucleotides, it has been shown that errors and deficiencies in a coded mRNA could be bypassed or removed from the mature gene transcripts.

In nature, the extent of genetic deletion or exon skipping in the splicing process is not fully understood, although many instances have been documented to occur, generally at very low levels (Sherrat TG, *et al.*, (1993) Am J Hum Genet 53, 1007-1015). However, it is recognised that if exons associated with disease-causing mutations can be specifically deleted from some genes, a shortened protein product can sometimes be produced that has similar biological properties of the native protein or has sufficient biological activity to ameliorate the disease caused by mutations associated with the target exon (Lu QL, *et al.*, (2003) Nature Medicine 9, 1009-1014; Aartsma-Rus A *et al.*, (2004) Am J Hum Genet 74: 83-92).

This process of targeted exon skipping is likely to be particularly useful in long genes where there are many exons and introns, where there is redundancy in the genetic constitution of the exons or where a protein is able to function without one or more

particular exons (*e.g.* with the dystrophin gene, which consists of 79 exons; or possibly some collagen genes which encode for repeated blocks of sequence or the huge nebulin or titin genes which are comprised of ~80 and over 370 exons, respectively).

Efforts to redirect gene processing for the treatment of genetic diseases associated with truncations caused by mutations in various genes have focused on the use of antisense oligonucleotides that either: (1) fully or partially overlap with the elements involved in the splicing process; or (2) bind to the pre-mRNA at a position sufficiently close to the element to disrupt the binding and function of the splicing factors that would normally mediate a particular splicing reaction which occurs at that element (*e.g.*, binds to the pre-mRNA at a position within 3, 6, or 9 nucleotides of the element to be blocked).

For example, modulation of mutant dystrophin pre-mRNA splicing with antisense oligoribonucleotides has been reported both *in vitro* and *in vivo*. In one type of dystrophin mutation reported in Japan, a 52-base pair deletion mutation causes exon 19 to be removed with the flanking introns during the splicing process (Matsuo *et al.*, (1991) J Clin Invest., 87:2127-2131). An *in vitro* minigene splicing system has been used to show that a 31-mer 2'-O-methyl oligoribonucleotide complementary to the 5' half of the deleted sequence in dystrophin Kobe exon 19 inhibited splicing of wild-type *pre-mRNA* (Takeshima *et al.* (1995), J. Clin. Invest., 95, 515-520). The same oligonucleotide was used to induce exon skipping from the native dystrophin gene transcript in human cultured lymphoblastoid cells.

Dunckley *et al.*, (1997) Nucleosides & Nucleotides, 16, 1665-1668 described *in vitro* constructs for analysis of splicing around exon 23 of mutated dystrophin in the *mdx* mouse mutant, a model for muscular dystrophy. Plans to analyse these constructs *in vitro* using 2' modified oligonucleotides targeted to splice sites within and adjacent to mouse dystrophin exon 23 were discussed, though no target sites or sequences were given.

2'-O-methyl oligoribonucleotides were subsequently reported to correct dystrophin deficiency in myoblasts from the *mdx* mouse from this group. An antisense oligonucleotide targeted to the 3' splice site of murine dystrophin intron 22 was reported to

cause skipping of the mutant exon as well as several flanking exons and created a novel in-frame dystrophin transcript with a novel internal deletion. This mutated dystrophin was expressed in 1-2% of antisense treated mdx myotubes. Use of other oligonucleotide modifications such as 2'-O-methoxyethyl phosphodiester are described (Dunckley *et al.* (1998) Human Mol. Genetics, 5, 1083-90).

Thus, antisense molecules may provide a tool in the treatment of genetic disorders such as Duchenne Muscular Dystrophy (DMD). However, attempts to induce exon skipping using antisense molecules have had mixed success. Studies on dystrophin exon 19, where successful skipping of that exon from the dystrophin pre-mRNA was achieved using a variety of antisense molecules directed at the flanking splice sites or motifs within the exon involved in exon definition as described by Errington *et al.* (2003) J Gen Med 5, 518-527".

In contrast to the apparent ease of exon 19 skipping, the first report of exon 23 skipping in the *mdx* mouse by Dunckley *et al.*, (1998) is now considered to be reporting only a naturally occurring revertant transcript or artefact rather than any true antisense activity. In addition to not consistently generating transcripts missing exon 23, Dunckley *et al.*, (1998) did not show any time course of induced exon skipping, or even titration of antisense oligonucleotides, to demonstrate dose dependent effects where the levels of exon skipping corresponded with increasing or decreasing amounts of antisense oligonucleotide. Furthermore, this work could not be replicated by other researchers.

The first example of specific and reproducible exon skipping in the *mdx* mouse model was reported by Wilton *et al.*, (1999) Neuromuscular Disorders 9, 330-338. By directing an antisense molecule to the donor splice site, consistent and efficient exon 23 skipping was induced in the dystrophin mRNA within 6 hours of treatment of the cultured cells. Wilton *et al.*, (1999), also describe targeting the acceptor region of the mouse dystrophin pre-mRNA with longer antisense oligonucleotides and being unable to repeat the published results of Dunckley *et al.*, (1998). No exon skipping, either 23 alone or multiple removal of several flanking exons, could be reproducibly detected using a selection of antisense oligonucleotides directed at the acceptor splice site of intron 22.

While the first antisense oligonucleotide directed at the intron 23 donor splice site induced consistent exon skipping in primary cultured myoblasts, this compound was found to be much less efficient in immortalized cell cultures expressing higher levels of dystrophin. However, with refined targeting and antisense oligonucleotide design, the efficiency of specific exon removal was increased by almost an order of magnitude (see Mann CJ *et al.*, (2002) J Gen Med 4, 644-654).

Thus, there remains a need to provide antisense oligonucleotides capable of binding to and modifying the splicing of a target nucleotide sequence. Simply directing the antisense oligonucleotides to motifs presumed to be crucial for splicing is no guarantee of the efficacy of that compound in a therapeutic setting.

#### SUMMARY OF THE INVENTION

The present invention provides antisense molecule compounds and compositions suitable for binding to RNA motifs involved in the splicing of pre-mRNA that are able to induce specific and efficient exon skipping and a method for their use thereof.

The choice of target selection plays a crucial role in the efficiency of exon skipping and hence its subsequent application of a potential therapy. Simply designing antisense molecules to target regions of pre-mRNA presumed to be involved in splicing is no guarantee of inducing efficient and specific exon skipping. The most obvious or readily defined targets for splicing intervention are the donor and acceptor splice sites although there are less defined or conserved motifs including exonic splicing enhancers, silencing elements and branch points.

The acceptor and donor splice sites have consensus sequences of about 16 and 8 bases respectively (see Figure 1 for schematic representation of motifs and domains involved in exon recognition, intron removal and the splicing process).

According to a first aspect, the invention provides antisense molecules capable of binding to a selected target to induce exon skipping.

For example, to induce exon skipping in exons 3 to 8, 10 to 16, 19 to 40, 42 to 44, 46, 47, and 50 to 53 in the Dystrophin gene transcript the antisense molecules are preferably selected from the group listed in Table 1A.

In a further example, it is possible to combine two or more antisense  
5 oligonucleotides of the present invention together to induce multiple exon skipping in exons 19-20, and 53. This is a similar concept to targeting of a single exon. A combination or "cocktail" of antisense oligonucleotides are directed at adjacent exons to induce efficient exon skipping.

In another example, to induce exon skipping in exons 19-20, 31, 34 and 53  
10 it is possible to improve exon skipping of a single exon by joining together two or more antisense oligonucleotide molecules. This concept is termed by the inventor as a "weasel", an example of a cunningly designed antisense oligonucleotide. A similar concept has been described in Aartsma-Rus A *et al.*, (2004) Am J Hum Genet 74: 83-92).

According to a second aspect, the present invention provides antisense  
15 molecules selected and or adapted to aid in the prophylactic or therapeutic treatment of a genetic disorder comprising at least an antisense molecule in a form suitable for delivery to a patient.

According to a third aspect, the invention provides a method for treating a  
patient suffering from a genetic disease wherein there is a mutation in a gene encoding a  
20 particular protein and the affect of the mutation can be abrogated by exon skipping, comprising the steps of: (a) selecting an antisense molecule in accordance with the methods described herein; and (b) administering the molecule to a patient in need of such treatment.

The invention also addresses the use of purified and isolated antisense  
oligonucleotides of the invention, for the manufacture of a medicament for treatment of a  
25 genetic disease.

The invention further provides a method of treating a condition  
characterised by Duchenne muscular dystrophy, which method comprises administering to  
a patient in need of treatment an effective amount of an appropriately designed antisense  
oligonucleotide of the invention, relevant to the particular genetic lesion in that patient.



Further, the invention provides a method for prophylactically treating a patient to prevent or at least minimise Duchene muscular dystrophy, comprising the step of: administering to the patient an effective amount of an antisense oligonucleotide or a pharmaceutical composition comprising one or more of these biological molecules.

5                   The invention also provides kits for treating a genetic disease, which kits comprise at least a antisense oligonucleotide of the present invention, packaged in a suitable container and instructions for its use.

                  Other aspects and advantages of the invention will become apparent to those skilled in the art from a review of the ensuing description, which proceeds with reference to  
10   the following figures.

#### BRIEF DESCRIPTION OF THE DRAWINGS

- Figure 1       Schematic representation of motifs and domains involved in exon recognition, intron removal and the splicing process (SEQ ID NOS: 213 and 214).
- 15   Figure 2       Diagrammatic representation of the concept of antisense oligonucleotide induced exon skipping to by-pass disease-causing mutations (not drawn to scale). The hatched box represents an exon carrying a mutation that prevents the translation of the rest of the mRNA into a protein. The solid black bar represents an antisense oligonucleotide that prevents inclusion of that exon in the mature mRNA.
- 20
- Figure 3       Gel electrophoresis showing differing efficiencies of two antisense molecules directed at exon 8 acceptor splice site. The preferred compound [H8A(-06+18)] induces strong and consistent exon skipping at a transfection concentration of 20 nanomolar in cultured normal human muscle cells. The less preferred antisense oligonucleotide [H8A(-06+14)] also induces
- 25               efficient exon skipping, but at much higher concentrations. Other antisense oligonucleotides directed at exon 8 either only induced lower levels of exon skipping or no detectable skipping at all (not shown).

- Figure 4 Gel electrophoresis showing differing efficiencies of two antisense molecules directed at internal domains within exon 7, presumably exon splicing enhancers. The preferred compound [H7A(+45+67)] induces strong and consistent exon skipping at a transfection concentration of 20 nanomolar in cultured human muscle cells. The less preferred antisense oligonucleotide [H7A(+2+26)] induces only low levels of exon skipping at the higher transfection concentrations. Other antisense oligonucleotides directed at exon 7 either only induced lower levels of exon skipping or no detectable skipping at all (not shown).
- 5
- 10 Figure 5 Gel electrophoresis showing an example of low efficiency exon 6 skipping using two non-preferred antisense molecules directed at human exon 6 donor splice site. Levels of induced exon 6 skipping are either very low [H6D(+04-21)] or almost undetectable [H6D(+18-04)]. These are examples of non-preferred antisense oligonucleotides to demonstrate that antisense oligonucleotide design plays a crucial role in the efficacy of these compounds.
- 15
- Figure 6 Gel electrophoresis showing strong and efficient human exon 6 skipping using an antisense molecules [H6A(+69+91)] directed at an exon 6 internal domain, presumably an exon splicing enhancer. This preferred compound induces consistent exon skipping at a transfection concentration of 20 nanomolar in cultured human muscle cells.
- 20
- Figure 7 Gel electrophoresis showing strong human exon 4 skipping using an antisense molecule H4A(+13+32) directed at an exon 6 internal domain, presumably an exon splicing enhancer. This preferred compound induces strong and consistent exon skipping at a transfection concentration of 20 nanomolar in cultured human muscle cells,
- 25
- Figure 8A Gel electrophoresis showing strong human exon 12 skipping using antisense molecule H12A(+52+75) directed at exon 12 internal domain.

- Figure 8B Gel electrophoresis showing strong human exon 11 skipping using antisense molecule H11A(+75+97) directed at an exon 11 internal domain.
- Figure 9A Gel electrophoresis showing strong human exon 15 skipping using antisense molecules H15A(+48+71) and H15A(-12+19) directed at an exon 15 internal domain.
- 5 Figure 9B Gel electrophoresis showing strong human exon 16 skipping using antisense molecules H16A(-12+19) and H16A(-06+25).
- Figure 10 Gel electrophoresis showing human exon 19/20 skipping using antisense molecules H20A(+44+71) and H20A(+149+170) directed at an exon 20 and a "cocktail" of antisense oligonucleotides H19A(+35+65, H20A(+44+71) and H20A(+149+170) directed at exons 19/20.
- 10 Figure 11 Gel electrophoresis showing human exon 19/20 skipping using "weasels" directed at exons 19 and 20.
- Figure 12 Gel electrophoresis showing exon 22 skipping using antisense molecules H22A(+125+106), H22A(+47+69), H22A(+80+101) and H22D(+13-11) directed at exon 22.
- 15 Figure 13 Gel electrophoresis showing exon 31 skipping using antisense molecules H31D(+01-25) and H31D(+03-22); and a "cocktail" of antisense molecules directed at exon 31.
- 20 Figure 14 Gel electrophoresis showing exon 33 skipping using antisense molecules H33A(+30+56) and H33A(+64+88) directed at exon 33.
- Figure 15 Gel electrophoresis showing exon 35 skipping using antisense molecules H35A(+141+161), H35A(+116+135), and H35A(+24+43) and a "cocktail of two antisense molecules, directed at exon 35.
- 25 Figure 16 Gel electrophoresis showing exon 36 skipping using antisense molecules H32A(+49+73) and H36A(+26+50) directed at exon 36.
- Figure 17 Gel electrophoresis showing exon 37 skipping using antisense molecules H37A(+82+105) and H37A(+134+157) directed at exon 37.

- Figure 18 Gel electrophoresis showing exon 38 skipping using antisense molecule H38A(+88+112) directed at exon 38.
- Figure 19 Gel electrophoresis showing exon 40 skipping using antisense molecule H40A(-05+17) directed at exon 40.
- 5 Figure 20 Gel electrophoresis showing exon 42 skipping using antisense molecule H42A(-04+23) directed at exon 42.
- Figure 21 Gel electrophoresis showing exon 46 skipping using antisense molecule H46A(+86+115) directed at exon 46
- Figure 22 Gel electrophoresis showing exon 51, exon 52 and exon 53 skipping using  
 10 various antisense molecules directed at exons 51, 52 and 53, respectively. A "cocktail" of antisense molecules is also shown directed at exon 53.

#### BRIEF DESCRIPTION OF THE SEQUENCE LISTINGS

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
1	H8A(-06+18)	GAU AGG UGG UAU CAA CAU CUG UAA
2	H8A (-03+18)	GAU AGG UGG UAU CAA CAU CUG
3	H8A(-07+18)	GAU AGG UGG UAU CAA CAU CUG UAA G
4	H8A(-06+14)	GGU GGU AUC AAC AUC UGU AA
5	H8A(-10+10)	GUA UCA ACA UCU GUA AGC AC
6	H7A(+45+67)	UGC AUG UUC CAG UCG UUG UGU GG
7	H7A(+02+26)	CAC UAU UCC AGU CAA AUA GGU CUG G
8	H7D(+15-10)	AUU UAC CAA CCU UCA GGA UCG AGU A
9	H7A(-18+03)	GGC CUA AAA CAC AUA CAC AUA
10	C6A(-10+10)	CAU UUU UGA CCU ACA UGU GG
11	C6A(-14+06)	UUU GAC CUA CAU GUG GAA AG
12	C6A(-14+12)	UAC AUU UUU GAC CUA CAU GUG GAA AG
13	C6A(-13+09)	AUU UUU GAC CUA CAU GGG AAA G
14	CH6A(+69+91)	UAC GAG UUG AUU GUC GGA CCC AG
15	C6D(+12-13)	GUG GUC UCC UUA CCU AUG ACU GUG G
16	C6D(+06-11)	GGU CUC CUU ACC UAU GA
17	H6D(+04-21)	UGU CUC AGU AAU CUU CUU ACC UAU
18	H6D(+18-04)	UCU UAC CUA UGA CUA UGG AUG AGA
19	H4A(+13+32)	GCA UGA ACU CUU GUG GAU CC
20	H4D(+04-16)	CCA GGG UAC UAC UUA CAU UA
21	H4D(-24-44)	AUC GUG UGU CAC AGC AUC CAG

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
22	H4A(+11+40)	UGU UCA GGG CAU GAA CUC UUG UGG AUC CUU
23	H3A(+30+60)	UAG GAG GCG CCU CCC AUC CUG UAG GUC ACU G
24	H3A(+35+65)	AGG UCU AGG AGG CGC CUC CCA UCC UGU AGG U
25	H3A(+30+54)	GCG CCU CCC AUC CUG UAG GUC ACU G
26	H3D(+46-21)	CUU CGA GGA GGU CUA GGA GGC GCC UC
27	H3A(+30+50)	CUC CCA UCC UGU AGG UCA CUG
28	H3D(+19-03)	UAC CAG UUU UUG CCC UGU CAG G
29	H3A(-06+20)	UCA AUA UGC UGC UUC CCA AAC UGA AA
30	H3A(+37+61)	CUA GGA GGC GCC UCC CAU CCU GUA G
31	H5A(+20+50)	UUA UGA UUU CCA UCU ACG AUG UCA GUA CUU C
32	H5D(+25-05)	CUU ACC UGC CAG UGG AGG AUU AUA UUC CAA A
33	H5D(+10-15)	CAU CAG GAU UCU UAC CUG CCA GUG G
34	H5A(+10+34)	CGA UGU CAG UAC UUC CAA UAU UCA C
35	H5D(-04-21)	ACC AUU CAU CAG GAU UCU
36	H5D(+16-02)	ACC UGC CAG UGG AGG AUU
37	H5A(-07+20)	CCA AUA UUC ACU AAA UCA ACC UGU UAA
38	H5D(+18-12)	CAG GAU UGU UAC CUG CCA GUG GAG GAU UAU
39	H5A(+05+35)	ACG AUG UCA GUA CUU CCA AUA UUC ACU AAA U
40	H5A(+15+45)	AUU UCC AUC UAC GAU GUC AGU ACU UCC AAU A
41	H10A(-05+16)	CAG GAG CUU CCA AAU GCU GCA
42	H10A(-05+24)	CUU GUC UUC AGG AGC UUC CAA AUG CUG CA
43	H10A(+98+119)	UCC UCA GCA GAA AGA AGC CAC G
44	H10A(+130+149)	UUA GAA AUC UCU CCU UGU GC
45	H10A(-33-14)	UAA AUU GGG UGU UAC ACA AU
46	H11D(+26+49)	CCC UGA GGC AUU CCC AUC UUG AAU
47	H11D(+11-09)	AGG ACU UAC UUG CUU UGU UU
48	H11A(+118+140)	CUU GAA UUU AGG AGA UUC AUC UG
49	H11A(+75+97)	CAU CUU CUG AUA AUU UUC CUG UU
50	H12A(+52+75)	UCU UCU GUU UUU GUU AGC CAG UCA
51	H12A(-10+10)	UCU AUG UAA ACU GAA AAU UU
52	H12A(+11+30)	UUC UGG AGA UCC AUU AAA AC
53	H13A(+77+100)	CAG CAG UUG CGU GAU CUC CAC UAG
54	H13A(+55+75)	UUC AUC AAC UAC CAC CAC CAU

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
55	H13D(+06-19)	CUA AGC AAA AUA AUC UGA CCU UAA G
56	H14A(+37+64)	CUU GUA AAA GAA CCC AGC GGU CUU CUG U
57	H14A(+14+35)	CAU CUA CAG AUG UUU GCC CAU C
58	H14A(+51+73)	GAA GGA UGU CUU GUA AAA GAA CC
59	H14D(-02+18)	ACC UGU UCU UCA GUA AGA CG
60	H14D(+14-10)	CAU GAC ACA CCU GUU CUU CAG UAA
61	H14A(+61+80)	CAU UUG AGA AGG AUG UCU UG
62	H14A(-12+12)	AUC UCC CAA UAC CUG GAG AAG AGA
63	H15A(-12+19)	GCC AUG CAC UAA AAA GGC ACU GCA AGA CAU U
64	H15A(+48+71)	UCU UUA AAG CCA GUU GUG UGA AUC
65	H15A(+08+28)	UUU CUG AAA GCC AUG CAC UAA
66	H15D(+17-08)	GUA CAU ACG GCC AGU UUU UGA AGA C
67	H16A(-12+19)	CUA GAU CCG CUU UUA AAA CCU GUU AAA ACA A
68	H16A(-06+25)	UCU UUU CUA GAU CCG CUU UUA AAA CCU GUU A
69	H16A(-06+19)	CUA GAU CCG CUU UUA AAA CCU GUU A
70	H16A(+87+109)	CCG UCU UCU GGG UCA CUG ACU UA
71	H16A(-07+19)	CUA GAU CCG CUU UUA AAA CCU GUU AA
72	H16A(-07+13)	CCG CUU UUA AAA CCU GUU AA
73	H16A(+12+37)	UGG AUU GCU UUU UCU UUU CUA GAU CC
74	H16A(+92+116)	CAU GCU UCC GUC UUC UGG GUC ACU G
75	H16A(+45+67)	G AUC UUG UUU GAG UGA AUA CAG U
76	H16A(+105+126)	GUU AUC CAG CCA UGC UUC CGU C
77	H16D(+05-20)	UGA UAA UUG GUA UCA CUA ACC UGU G
78	H16D(+12-11)	GUA UCA CUA ACC UGU GCU GUA C
79	H19A(+35+53)	CUG CUG GCA UCU UGC AGU U
80	H19A(+35+65)	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U
81	H20A(+44+71)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C
82	H20A(+147+168)	CAG CAG UAG UUG UCA UCU GCU C
83	H20A(+185+203)	UGA UGG GGU GGU GGG UUG G
84	H20A(-08+17)	AUC UGC AUU AAC ACC CUC UAG AAA G
85	H20A(+30+53)	CCG GCU GUU CAG UUG UUC UGA GGC
86	H20A(-11+17)	AUC UGC AUU AAC ACC CUC UAG AAA GAA A
87	H20D(+08-20)	GAA GGA GAA GAG AUU CUU ACC UUA CAA A
88	H20A(+44+63)	AUU CGA UCC ACC GGC UGU UC
89	H20A(+149+168)	CAG CAG UAG UUG UCA UCU GC
90	H21A(-06+16)	GCC GGU UGA CUU CAU CCU GUG C
91	H21A(+85+106)	CUG CAU CCA GGA ACA UGG GUC C



SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
92	H21A(+85+108)	GUC UGC AUC CAG GAA CAU GGG UC
93	H21A(+08+31)	GUU GAA GAU CUG AUA GCC GGU UGA
94	H21D(+18-07)	UAC UUA CUG UCU GUA GCU CUU UCU
95	H22A(+22+45)	CAC UCA UGG UCU CCU GAU AGC GCA
96	H22A(+125+106)	CUG CAA UUC CCC GAG UCU CUG C
97	H22A(+47+69)	ACU GCU GGA CCC AUG UCC UGA UG
98	H22A(+80+101)	CUA AGU UGA GGU AUG GAG AGU
99	H22D(+13-11)	UAU UCA CAG ACC UGC AAU UCC CC
100	H23A(+34+59)	ACA GUG GUG CUG AGA UAG UAU AGG CC
101	H23A(+18+39)	UAG GCC ACU UUG UUG CUC UUG C
102	H23A(+72+90)	UUC AGA GGG CGC UUU CUU C
103	H24A(+48+70)	GGG CAG GCC AUU CCU CCU UCA GA
104	H24A(-02+22)	UCU UCA GGG UUU GUA UGU GAU UCU
105	H25A(+9+36)	CUG GGC UGA AUU GUC UGA AUA UCA CUG
106	H25A(+131+156)	CUG UUG GCA CAU GUG AUC CCA CUG AG
107	H25D(+16-08)	GUC UAU ACC UGU UGG CAC AUG UGA
108	H26A(+132+156)	UGC UUU CUG UAA UUC AUC UGG AGU U
109	H26A(-07+19)	CCU CCU UUC UGG CAU AGA CCU UCC AC
110	H26A(+68+92)	UGU GUC AUC CAU UCG UGC AUC UCU G
111	H27A(+82+106)	UUA AGG CCU CUU GUG CUA CAG GUG G
112	H27A(-4+19)	GGG GCU CUU CUU UAG CUC UCU GA
113	H27D(+19-03)	GAC UUC CAA AGU CUU GCA UUU C
114	H28A(-05+19)	GCC AAC AUG CCC AAA CUU CCU AAG
115	H28A(+99+124)	CAG AGA UUU CCU CAG CUC CGC CAG GA
116	H28D(+16-05)	CUU ACA UCU AGC ACC UCA GAG
117	H29A(+57+81)	UCC GCC AUC UGU UAG GGU CUG UGC C
118	H29A(+18+42)	AUU UGG GUU AUC CUC UGA AUG UCG C
119	H29D(+17-05)	CAU ACC UCU UCA UGU AGU UCC C
120	H30A(+122+147)	CAU UUG AGC UGC GUC CAC CUU GUC UG
121	H30A(+25+50)	UCC UGG GCA GAC UGG AUG CUC UGU UC
122	H30D(+19-04)	UUG CCU GGG CUU CCU GAG GCA UU
123	H31D(+06-18)	UUC UGA AAU AAC AUA UAC CUG UGC
124	H31D(+03-22)	UAG UUU CUG AAA UAA CAU AUA CCU G
125	H31A(+05+25)	GAC UUG UCA AAU CAG AUU GGA
126	H31D(+04-20)	GUU UCU GAA AUA ACA UAU ACC UGU
127	H32D(+04-16)	CAC CAG AAA UAC AUA CCA CA
128	H32A(+151+170)	CAA UGA UUU AGC UGU GAC UG
129	H32A(+10+32)	CGA AAC UUC AUG GAG ACA UCU UG
130	H32A(+49+73)	CUU GUA GAC GCU GCU CAA AAU UGG C
131	H33D(+09-11)	CAU GCA CAC ACC UUU GCU CC
132	H33A(+53+76)	UCU GUA CAA UCU GAC GUC CAG UCU

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
133	H33A(+30+56)	GUC UUU AUC ACC AUU UCC ACU UCA GAC
134	H33A(+64+88)	CCG UCU GCU UUU UCU GUA CAA UCU G
135	H34A(+83+104)	UCC AUA UCU GUA GCU GCC AGC C
136	H34A(+143+165)	CCA GGC AAC UUC AGA AUC CAA AU
137	H34A(-20+10)	UUU CUG UUA CCU GAA AAG AAU UAU AAU GAA
138	H34A(+46+70)	CAU UCA UUU CCU UUC GCA UCU UAC G
139	H34A(+95+120)	UGA UCU CUU UGU CAA UUC CAU AUC UG
140	H34D(+10-20)	UUC AGU GAU AUA GGU UUU ACC UUU CCC CAG
141	H34A(+72+96)	CUG UAG CUG CCA GCC AUU CUG UCA AG
142	H35A(+141+161)	UCU UCU GCU CGG GAG GUG ACA
143	H35A(+116+135)	CCA GUU ACU AUU CAG AAG AC
144	H35A(+24+43)	UCU UCA GGU GCA CCU UCU GU
145	H36A(+26+50)	UGU GAU GUG GUC CAC AUU CUG GUC A
146	H36A(-02+18)	CCA UGU GUU UCU GGU AUU CC
147	H37A(+26+50)	CGU GUA GAG UCC ACC UUU GGG CGU A
148	H37A(+82+105)	UAC UAA UUU CCU GCA GUG GUC ACC
149	H37A(+134+157)	UUC UGU GUG AAA UGG CUG CAA AUC
150	H38A(-01+19)	CCU UCA AAG GAA UGG AGG CC
151	H38A(+59+83)	UGC UGA AUU UCA GCC UCC AGU GGU U
152	H38A(+88+112)	UGA AGU CUU CCU CUU UCA GAU UCA C
153	H39A(+62+85)	CUG GCU UUC UCU CAU CUG UGA UUC
154	H39A(+39+58)	GUU GUA AGU UGU CUC CUC UU
155	H39A(+102+121)	UUG UCU GUA ACA GCU GCU GU
156	H39D(+10-10)	GCU CUA AUA CCU UGA GAG CA
157	H40A(-05+17)	CUU UGA GAC CUC AAA UCC UGU U
158	H40A(+129+153)	CUU UAU UUU CCU UUC AUC UCU GGG C
159	H42A(-04+23)	AUC GUU UCU UCA CGG ACA GUG UGC UGG
160	H42A(+86+109)	GGG CUU GUG AGA CAU GAG UGA UUU
161	H42D(+19-02)	A CCU UCA GAG GAC UCC UCU UGC
162	H43D(+10-15)	UAU GUG UUA CCU ACC CUU GUC GGU C
163	H43A(+101+120)	GGA GAG AGC UUC CUG UAG CU
164	H43A(+78+100)	UCA CCC UUU CCA CAG GCG UUG CA
165	H44A(+85+104)	UUU GUG UCU UUC UGA GAA AC
166	H44D(+10-10)	AAA GAC UUA CCU UAA GAU AC
167	H44A(-06+14)	AUC UGU CAA AUC GCC UGC AG
168	H46D(+16-04)	UUA CCU UGA CUU GCU CAA GC
169	H46A(+90+109)	UCC AGG UUC AAG UGG GAU AC
170	H47A(+76+100)	GCU CUU CUG GGC UUA UGG GAG CAC U
171	H47D(+25-02)	ACC UUU AUC CAC UGG AGA UUU GUC UGC

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
172	H47A(-9+12)	UUC CAC CAG UAA CUG AAA CAG
173	H50A(+02+30)	CCA CUC AGA GCU CAG AUC UUC UAA CUU CC
174	H50A(+07+33)	CUU CCA CUC AGA GCU CAG AUC UUC UAA
175	H50D(+07-18)	GGG AUC CAG UAU ACU UAC AGG CUC C
176	H51A(-01+25)	ACC AGA GUA ACA GUC UGA GUA GGA GC
177	H51D(+16-07)	CUC AUA CCU UCU GCU UGA UGA UC
178	H51A(+111 +134)	UUC UGU CCA AGC CCG GUU GAA AUC
179	H51A(+61+90)	ACA UCA AGG AAG AUG GCA UUU CUA GUU UGG
180	H51A(+66+90)	ACA UCA AGG AAG AUG GCA UUU CUA G
181	H51A(+66+95)	CUC CAA CAU CAA GGA AGA UGG CAU UUC UAG
182	H51D(+08-17)	AUC AUU UUU UCU CAU ACC UUC UGC U
183	H51A/D(+08-17) & (-15+)	AUC AUU UUU UCU CAU ACC UUC UGC UAG GAG CUA AAA
184	H51A(+175+195)	CAC CCA CCA UCA CCC UCU GUG
185	H51A(+199+220)	AUC AUC UCG UUG AUA UCC UCA A
186	H52A(-07+14)	UCC UGC AUU GUU GCC UGU AAG
187	H52A(+12+41)	UCC AAC UGG GGA CGC CUC UGU UCC AAA UCC
188	H52A(+17+37)	ACU GGG GAC GCC UCU GUU CCA
189	H52A(+93+112)	CCG UAA UGA UUG UUC UAG CC
190	H52D(+05-15)	UGU UAA AAA ACU UAC UUC GA
191	H53A(+45+69)	CAU UCA ACU GUU GCC UCC GGU UCU G
192	H53A(+39+62)	CUG UUG CCU CCG GUU CUG AAG GUG
193	H53A(+39+69)	CAU UCA ACU GUU GCC UCC GGU UCU GAA GGU G
194	H53D(+14-07)	UAC UAA CCU UGG UUU CUG UGA
195	H53A(+23+47)	CUG AAG GUG UUC UUG UAC UUC AUC C
196	H53A(+150+176)	UGU AUA GGG ACC CUC CUU CCA UGA CUC
197	H53D(+20-05)	CUA ACC UUG GUU UCU GUG AUU UUC U
198	H53D(+09-18)	GGU AUC UUU GAU ACU AAC CUU GGU UUC
199	H53A(-12+10)	AUU CUU UCA ACU AGA AUA AAA G
200	H53A(-07+18)	GAU UCU GAA UUC UUU CAA CUA GAA U
201	H53A(+07+26)	AUC CCA CUG AUU CUG AAU UC
202	H53A(+124+145)	UUG GCU CUG GCC UGU CCU AAG A
203	H46A(+86+115)	CUC UUU UCC AGG UUC AAG UGG GAU ACU AGC
204	H46A(+107+137)	CAA GCU UUU CUU UUA GUU GCU GCU CUU UUC C
205	H46A(-10+20)	UAU UCU UUU GUU CUU CUA GCC UGG AGA

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5' - 3')
		AAG
206	H46A(+50+77)	CUG CUU CCU CCA ACC AUA AAA CAA AUU C
207	H45A(-06+20)	CCA AUG CCA UCC UGG AGU UCC UGU AA
208	H45A(+91 +110)	UCC UGU AGA AUA CUG GCA UC
209	H45A(+125+151)	UGC AGA CCU CCU GCC ACC GCA GAU UCA
210	H45D(+16 -04)	CUA CCU CUU UUU UCU GUC UG
211	H45A(+71+90)	UGU UUU UGA GGA UUG CUG AA

**Table 1A:** Description of 2'-O-methyl phosphorothioate antisense oligonucleotides that have been used to date to study induced exon skipping during the processing of the dystrophin pre-mRNA. Since these 2'-O-methyl antisense oligonucleotides are more RNA-like, U represents uracil. With other antisense chemistries such as peptide nucleic acids or morpholinos, these U bases may be shown as "T".

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5'-3')
81 82	H20A(+44+71) H20A(+147+168)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C CAG CAG UAG UUG UCA UCU GCU C
80 81 82	H19A(+35+65) H20A(+44+71) H20A(+147+168)	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U CUG GCA GAA UUC GAU CCA CCG GCU GUU C CAG CAG UAG UUG UCA UCU GCU C
194 195 196	H53D(+14-07) H53A(+23+47) H53A(+150+175)	UAC UAA CCU UGG UUU CUG UGA CUG AAG GUG UUC UUG UAC UUC AUC C UGU AUA GGG ACC CUC CUU CCA UGA CUC

**Table 1B:** Description of a cocktail of 2'-O-methyl phosphorothioate antisense oligonucleotides that have been used to date to study induced exon skipping during the processing of the dystrophin pre-mRNA.

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5'-3')
81 82	H20A(+44+71)- H20A(+147+168)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C- CAG CAG UAG UUG UCA UCU GCU C
80	H19A(+35+65)-	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U
88	H20A(+44+63)-	-AUU CGA UCC ACC GGC UGU UC-

SEQ ID	SEQUENCE	NUCLEOTIDE SEQUENCE (5'-3')
79	H20A(+149+168)	CUG CUG GCA UCU UGC AGU U
80	H19A(+35+65)-	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U
88	H20A(+44+63)	-AUU CGA UCC ACC GGC UGU UC-
80	H19A(+35+65)-	GCC UGA GCU GAU CUG CUG GCA UCU UGC AGU U
79	H20A(+149+168)	-CUG CUG GCA UCU UGC AGU U
138	H34A(+46+70)-	CAU UCA UUU CCU UUC GCA UCU UAC G-
139	H34A(+94+120)	UGA UCU CUU UGU CAA UUC CAU AUC UG
124	H31D(+03-22)-	UAG UUU CUG AAA UAA CAU AUA CCU G-
144	H35A(+24+43)	UU- UCU UCA GGU GCA CCU UCU GU
195	H53A(+23+47)-	CUG AAG GUG UUC UUG UAC UUC AUC C-
196	H53A(+150+175)-	AA- UGU AUA GGG ACC CUC CUU CCA UGA CUC-
194	H53D(+14-07)	AA- UAC UAA CCU UGG UUU CUG UGA
- 212	Aimed at exons 19/20/20	CAG CAG UAG UUG UCA UCU GCU CAA CUG GCA GAA UUC GAU CCA CCG GCU GUU CAA GCC UGA GCU GAU CUG CUC GCA UCU UGC AGU

**Table 1C:** Description of a "weasel" of 2'-O-methyl phosphorothioate antisense oligonucleotides that have been used to date to study induced exon skipping during the processing of the dystrophin pre-mRNA.

## DETAILED DESCRIPTION OF THE INVENTION

### 5 General

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the invention includes all such variation and modifications. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in the specification, individually or collectively and any and all combinations or any two or more of the steps or features.

The present invention is not to be limited in scope by the specific embodiments described herein, which are intended for the purpose of exemplification only. Functionally equivalent products, compositions and methods are clearly within the scope of the invention as described herein.

5                      Sequence identity numbers (SEQ ID NO:) containing nucleotide and amino acid sequence information included in this specification are collected at the end of the description and have been prepared using the programme PatentIn Version 3.0. Each nucleotide or amino acid sequence is identified in the sequence listing by the numeric indicator <210> followed by the sequence identifier (*e.g.* <210>1, <210>2, etc.). The  
10   length, type of sequence and source organism for each nucleotide or amino acid sequence are indicated by information provided in the numeric indicator fields <211>, <212> and <213>, respectively. Nucleotide and amino acid sequences referred to in the specification are defined by the information provided in numeric indicator field <400> followed by the sequence identifier (*e.g.* <400>1, <400>2, etc.).

15 An antisense molecules nomenclature system was proposed and published to distinguish between the different antisense molecules (see Mann *et al.*, (2002) J Gen Med 4, 644-654). This nomenclature became especially relevant when testing several slightly different antisense molecules, all directed at the same target region, as shown below:

20 H # A/D (x : y).

The first letter designates the species (*e.g.* H: human, M: murine, C: canine)  
"#" designates target dystrophin exon number.

"A/D" indicates acceptor or donor splice site at the beginning and end of the exon, respectively.

25 (x y) represents the annealing coordinates where "-" or "+" indicate intronic or exonic sequences respectively. As an example, A(-6+18) would indicate the last 6 bases of the intron preceding the target exon and the first 18 bases of the target exon. The closest splice site would be the acceptor so these coordinates would be preceded with an "A". Describing annealing coordinates at the donor splice site could be D(+2-18) where the last



2 exonic bases and the first 18 intronic bases correspond to the annealing site of the antisense molecule. Entirely exonic annealing coordinates that would be represented by A(+65+85), that is the site between the 65th and 85th nucleotide from the start of that exon.

The entire disclosures of all publications (including patents, patent applications, journal articles, laboratory manuals, books, or other documents) cited herein are hereby incorporated by reference. No admission is made that any of the references constitute prior art or are part of the common general knowledge of those working in the field to which this invention relates.

As used necessarily herein the term "derived" and "derived from" shall be taken to indicate that a specific integer may be obtained from a particular source *albeit* not directly from that source.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

Other definitions for selected terms used herein may be found within the detailed description of the invention and apply throughout. Unless otherwise defined, all other scientific and technical terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which the invention belongs.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

When antisense molecule(s) are targeted to nucleotide sequences involved in splicing in exons within pre-mRNA sequences, normal splicing of the exon may be inhibited causing the splicing machinery to by-pass the entire mutated exon from the mature mRNA. The concept of antisense oligonucleotide induced exon skipping is shown in Figure 2. In many genes, deletion of an entire exon would lead to the production of a non-functional protein through the loss of important functional domains or the disruption of the reading frame. In some proteins, however, it is possible to shorten the protein by deleting one or more exons, without disrupting the reading frame, from within the protein

without seriously altering the biological activity of the protein. Typically, such proteins have a structural role and or possess functional domains at their ends. The present invention describes antisense molecules capable of binding to specified dystrophin pre-mRNA targets and re-directing processing of that gene.

5 Antisense Molecules

According to a first aspect of the invention, there is provided antisense molecules capable of binding to a selected target to induce exon skipping. To induce exon skipping in exons of the Dystrophin gene transcript, the antisense molecules are preferably selected from the group of compounds shown in Table 1A. There is also provided a  
10 combination or "cocktail" of two or more antisense oligonucleotides capable of binding to a selected target to induce exon skipping. To induce exon skipping in exons of the Dystrophin gene transcript, the antisense molecules in a "cocktail" are preferably selected from the group of compounds shown in Table 1B. Alternatively, exon skipping may be induced by antisense oligonucleotides joined together "weasels" preferably selected from  
15 the group of compounds shown in Table 1C.

Designing antisense molecules to completely mask consensus splice sites may not necessarily generate any skipping of the targeted exon. Furthermore, the inventors have discovered that size or length of the antisense oligonucleotide itself is not always a primary factor when designing antisense molecules. With some targets such as exon 19,  
20 antisense oligonucleotides as short as 12 bases were able to induce exon skipping, *albeit* not as efficiently as longer (20-31 bases) oligonucleotides. In some other targets, such as murine dystrophin exon 23, antisense oligonucleotides only 17 residues long were able to induce more efficient skipping than another overlapping compound of 25 nucleotides.

The inventors have also discovered that there does not appear to be any  
25 standard motif that can be blocked or masked by antisense molecules to redirect splicing. In some exons, such as mouse dystrophin exon 23, the donor splice site was the most amenable to target to re-direct skipping of that exon. It should be noted that designing and testing a series of exon 23 specific antisense molecules to anneal to overlapping regions of

the donor splice site showed considerable variation in the efficacy of induced exon skipping. As reported in Mann *et al.*, (2002) there was a significant variation in the efficiency of bypassing the nonsense mutation depending upon antisense oligonucleotide annealing ("Improved antisense oligonucleotide induced exon skipping in the *mdx* mouse model of muscular dystrophy". *J Gen Med* 4: 644-654). Targeting the acceptor site of exon 23 or several internal domains was not found to induce any consistent exon 23 skipping.

In other exons targeted for removal, masking the donor splice site did not induce any exon skipping. However, by directing antisense molecules to the acceptor splice site (human exon 8 as discussed below), strong and sustained exon skipping was induced. It should be noted that removal of human exon 8 was tightly linked with the co-removal of exon 9. There is no strong sequence homology between the exon 8 antisense oligonucleotides and corresponding regions of exon 9 so it does not appear to be a matter of cross reaction. Rather the splicing of these two exons is inextricably linked. This is not an isolated instance as the same effect is observed in canine cells where targeting exon 8 for removal also resulted in the skipping of exon 9. Targeting exon 23 for removal in the mouse dystrophin pre-mRNA also results in the frequent removal of exon 22 as well. This effect occurs in a dose dependent manner and also indicates close coordinated processing of 2 adjacent exons.

In other targeted exons, antisense molecules directed at the donor or acceptor splice sites did not induce exon skipping while annealing antisense molecules to intra-exonic regions (*i.e.* exon splicing enhancers within human dystrophin exon 6) was most efficient at inducing exon skipping. Some exons, both mouse and human exon 19 for example, are readily skipped by targeting antisense molecules to a variety of motifs. That is, targeted exon skipping is induced after using antisense oligonucleotides to mask donor and acceptor splice sites or exon splicing enhancers.

To identify and select antisense oligonucleotides suitable for use in the modulation of exon skipping, a nucleic acid sequence whose function is to be modulated must first be identified. This may be, for example, a gene (or mRNA transcribed from the

gene) whose expression is associated with a particular disorder or disease state, or a nucleic acid molecule from an infectious agent. Within the context of the present invention, preferred target site(s) are those involved in mRNA splicing (*i.e.* splice donor sites, splice acceptor sites, or exonic splicing enhancer elements). Splicing branch points and exon recognition sequences or splice enhancers are also potential target sites for modulation of mRNA splicing.

Preferably, the present invention aims to provide antisense molecules capable of binding to a selected target in the dystrophin pre-mRNA to induce efficient and consistent exon skipping. Duchenne muscular dystrophy arises from mutations that preclude the synthesis of a functional dystrophin gene product. These Duchenne muscular dystrophy gene defects are typically nonsense mutations or genomic rearrangements such as deletions, duplications or micro-deletions or insertions that disrupt the reading frame. As the human dystrophin gene is a large and complex gene with the 79 exons being spliced together to generate a mature mRNA with an open reading frame of approximately 11,000 bases, there are many positions where these mutations can occur. Consequently, a comprehensive antisense oligonucleotide based therapy to address many of the different disease-causing mutations in the dystrophin gene will require that many exons can be targeted for removal during the splicing process.

Within the context of the present invention, preferred target site(s) are those involved in mRNA splicing (*i.e.* splice donor sites, splice acceptor sites or exonic splicing enhancer elements). Splicing branch points and exon recognition sequences or splice enhancers are also potential target sites for modulation of mRNA splicing.

The oligonucleotide and the DNA or RNA are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides which can hydrogen bond with each other. Thus, "specifically hybridisable" and "complementary" are terms which are used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the oligonucleotide and the DNA or RNA target. It is understood in the art that the sequence of an antisense molecule need not be 100% complementary to that of its target sequence to

be specifically hybridisable. An antisense molecule is specifically hybridisable when binding of the compound to the target DNA or RNA molecule interferes with the normal function of the target DNA or RNA to cause a loss of utility, and there is a sufficient degree of complementarity to avoid non-specific binding of the antisense compound to non-target sequences under conditions in which specific binding is desired, *i.e.*, under physiological conditions in the case of *in vivo* assays or therapeutic treatment, and in the case of *in vitro* assays, under conditions in which the assays are performed.

While the above method may be used to select antisense molecules capable of deleting any exon from within a protein that is capable of being shortened without affecting its biological function, the exon deletion should not lead to a reading frame shift in the shortened transcribed mRNA. Thus, if in a linear sequence of three exons the end of the first exon encodes two of three nucleotides in a codon and the next exon is deleted then the third exon in the linear sequence must start with a single nucleotide that is capable of completing the nucleotide triplet for a codon. If the third exon does not commence with a single nucleotide there will be a reading frame shift that would lead to the generation of truncated or a non-functional protein.

It will be appreciated that the codon arrangements at the end of exons in structural proteins may not always break at the end of a codon, consequently there may be a need to delete more than one exon from the pre-mRNA to ensure in-frame reading of the mRNA. In such circumstances, a plurality of antisense oligonucleotides may need to be selected by the method of the invention wherein each is directed to a different region responsible for inducing splicing in the exons that are to be deleted.

The length of an antisense molecule may vary so long as it is capable of binding selectively to the intended location within the pre-mRNA molecule. The length of such sequences can be determined in accordance with selection procedures described herein. Generally, the antisense molecule will be from about 10 nucleotides in length up to about 50 nucleotides in length. It will be appreciated however that any length of nucleotides within this range may be used in the method. Preferably, the length of the antisense molecule is between 17 to 30 nucleotides in length.



In order to determine which exons can be connected in a dystrophin gene, reference should be made to an exon boundary map. Connection of one exon with another is based on the exons possessing the same number at the 3' border as is present at the 5' border of the exon to which it is being connected. Therefore, if exon 7 were deleted, exon 5 6 must connect to either exons 12 or 18 to maintain the reading frame. Thus, antisense oligonucleotides would need to be selected which redirected splicing for exons 7 to 11 in the first instance or exons 7 to 17 in the second instance. Another and somewhat simpler approach to restore the reading frame around an exon 7 deletion would be to remove the two flanking exons. Induction of exons 6 and 8 skipping should result in an in-frame 10 transcript with the splicing of exons 5 to 9. In practise however, targeting exon 8 for removal from the pre-mRNA results in the co-removal of exon 9 so the resultant transcript would have exon 5 joined to exon 10. The inclusion or exclusion of exon 9 does not alter the reading frame. Once the antisense molecules to be tested have been identified, they are prepared according to standard techniques known in the art. The most common method for 15 producing antisense molecules is the methylation of the 2' hydroxyribose position and the incorporation of a phosphorothioate backbone produces molecules that superficially resemble RNA but that are much more resistant to nuclease degradation.

To avoid degradation of pre-mRNA during duplex formation with the antisense molecules, the antisense molecules used in the method may be adapted to 20 minimise or prevent cleavage by endogenous RNase H. This property is highly preferred as the treatment of the RNA with the unmethylated oligonucleotides either intracellularly or in crude extracts that contain RNase H leads to degradation of the pre-mRNA: antisense oligonucleotide duplexes. Any form of modified antisense molecules that is capable of bypassing or not inducing such degradation may be used in the present method. An example 25 of antisense molecules which when duplexed with RNA are not cleaved by cellular RNase H is 2'-O-methyl derivatives. 2'-O-methyl-oligoribonucleotides are very stable in a cellular environment and in animal tissues, and their duplexes with RNA have higher T<sub>m</sub> values than their ribo- or deoxyribo- counterparts.

Antisense molecules that do not activate RNase H can be made in accordance with known techniques (*see, e.g.*, U.S. Pat. 5,149,797). Such antisense molecules, which may be deoxyribonucleotide or ribonucleotide sequences, simply contain any structural modification which sterically hinders or prevents binding of RNase H to a duplex molecule containing the oligonucleotide as one member thereof, which structural modification does not substantially hinder or disrupt duplex formation. Because the portions of the oligonucleotide involved in duplex formation are substantially different from those portions involved in RNase H binding thereto, numerous antisense molecules that do not activate RNase H are available. For example, such antisense molecules may be oligonucleotides wherein at least one, or all, of the inter-nucleotide bridging phosphate residues are modified phosphates, such as methyl phosphonates, methyl phosphorothioates, phosphoromorpholidates, phosphoropiperazidates and phosphoramidates. For example, every other one of the internucleotide bridging phosphate residues may be modified as described. In another non-limiting example, such antisense molecules are molecules wherein at least one, or all, of the nucleotides contain a 2' lower alkyl moiety (*e.g.*, C<sub>1</sub>-C<sub>4</sub>, linear or branched, saturated or unsaturated alkyl, such as methyl, ethyl, ethenyl, propyl, 1-propenyl, 2-propenyl, and isopropyl). For example, every other one of the nucleotides may be modified as described.

While antisense oligonucleotides are a preferred form of the antisense molecules, the present invention comprehends other oligomeric antisense molecules, including but not limited to oligonucleotide mimetics such as are described below.

Specific examples of preferred antisense compounds useful in this invention include oligonucleotides containing modified backbones or non-natural inter-nucleoside linkages. As defined in this specification, oligonucleotides having modified backbones include those that retain a phosphorus atom in the backbone and those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified oligonucleotides that do not have a phosphorus atom in their inter-nucleoside backbone can also be considered to be oligonucleosides.

In other preferred oligonucleotide mimetics, both the sugar and the inter-nucleoside linkage, *i.e.*, the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleo-bases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone.

Modified oligonucleotides may also contain one or more substituted sugar moieties. Oligonucleotides may also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. Certain nucleo-bases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2°C and are presently preferred base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications.

Another modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates that enhance the activity, cellular distribution or cellular uptake of the oligonucleotide. Such moieties include but are not limited to lipid moieties such as a cholesterol moiety, cholic acid, a thioether, *e.g.*, hexyl-S-tritylthiol, a thiocholesterol, an aliphatic chain, *e.g.*, dodecandiol or undecyl residues, a phospholipid, *e.g.*, di-hexadecyl-rac-glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate, a polyamine or a polyethylene glycol chain, or adamantane acetic acid, a palmityl moiety, or an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety.

It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be

incorporated in a single compound or even at a single nucleoside within an oligonucleotide. The present invention also includes antisense compounds that are chimeric compounds. "Chimeric" antisense compounds or "chimeras," in the context of this invention, are antisense molecules, particularly oligonucleotides, which contain two or more chemically distinct regions, each made up of at least one monomer unit, *i.e.*, a nucleotide in the case of an oligonucleotide compound. These oligonucleotides typically contain at least one region wherein the oligonucleotide is modified so as to confer upon the increased resistance to nuclease degradation, increased cellular uptake, and an additional region for increased binding affinity for the target nucleic acid.

10 Methods of Manufacturing Antisense Molecules

The antisense molecules used in accordance with this invention may be conveniently and routinely made through the well-known technique of solid phase synthesis. Equipment for such synthesis is sold by several vendors including, for example, Applied Biosystems (Foster City, Calif.). One method for synthesising oligonucleotides on a modified solid support is described in U.S. Pat. No. 4,458,066.

Any other means for such synthesis known in the art may additionally or alternatively be employed. It is well known to use similar techniques to prepare oligonucleotides such as the phosphorothioates ~ and alkylated derivatives. In one such automated embodiment, diethyl-phosphoramidites are used as starting materials and may be synthesized as described by Beaucage, *et al.*, (1981) *Tetrahedron Letters*, 22:1859-1862.

The antisense molecules of the invention are synthesised *in vitro* and do not include antisense compositions of biological origin, or genetic vector constructs designed to direct the *in vivo* synthesis of antisense molecules. The molecules of the invention may also be mixed, encapsulated, conjugated or otherwise associated with other molecules, molecule structures or mixtures of compounds, as for example, liposomes, receptor targeted molecules, oral, rectal, topical or other formulations, for assisting in uptake, distribution and/or absorption.



### Therapeutic Agents

The present invention also can be used as a prophylactic or therapeutic, which may be utilised for the purpose of treatment of a genetic disease.

Accordingly, in one embodiment the present invention provides antisense  
5 molecules that bind to a selected target in the dystrophin pre-mRNA to induce efficient and consistent exon skipping described herein in a therapeutically effective amount admixed with a pharmaceutically acceptable carrier, diluent, or excipient.

The phrase "pharmaceutically acceptable" refers to molecular entities and compositions that are physiologically tolerable and do not typically produce an allergic or  
10 similarly untoward reaction, such as gastric upset and the like, when administered to a patient. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the compound is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water or saline solutions and  
15 aqueous dextrose and glycerol solutions are preferably employed as carriers, particularly for injectable solutions. Suitable pharmaceutical carriers are described in Martin, *Remington's Pharmaceutical Sciences*, 18th Ed., Mack Publishing Co., Easton, PA, (1990).

In a more specific form of the invention there are provided pharmaceutical compositions comprising therapeutically effective amounts of an antisense molecule  
20 together with pharmaceutically acceptable diluents, preservatives, solubilizers, emulsifiers, adjuvants and/or carriers. Such compositions include diluents of various buffer content (*e.g.*, Tris-HCl, acetate, phosphate), pH and ionic strength and additives such as detergents and solubilizing agents (*e.g.*, Tween 80, Polysorbate 80), anti-oxidants (*e.g.*, ascorbic acid, sodium metabisulfite), preservatives (*e.g.*, Thimersol, benzyl alcohol) and bulking  
25 substances (*e.g.*, lactose, mannitol). The material may be incorporated into particulate preparations of polymeric compounds such as polylactic acid, polyglycolic acid, etc. or into liposomes. Hylauronic acid may also be used. Such compositions may influence the physical state, stability, rate of *in vivo* release, and rate of *in vivo* clearance of the present proteins and derivatives. See, *e.g.*, Martin, *Remington's Pharmaceutical Sciences*, 18th Ed.

(1990, Mack Publishing Co., Easton, PA 18042) pages 1435-1712 that are herein incorporated by reference. The compositions may be prepared in liquid form, or may be in dried powder, such as lyophilised form.

5 It will be appreciated that pharmaceutical compositions provided according to the present invention may be administered by any means known in the art. Preferably, the pharmaceutical compositions for administration are administered by injection, orally, or by the pulmonary, or nasal route. The antisense molecules are more preferably delivered by intravenous, intra-arterial, intraperitoneal, intramuscular, or subcutaneous routes of administration.

10 Antisense molecule based therapy

Also addressed by the present invention is the use of antisense molecules of the present invention, for manufacture of a medicament for modulation of a genetic disease.

15 The delivery of a therapeutically useful amount of antisense molecules may be achieved by methods previously published. For example, intracellular delivery of the antisense molecule may be via a composition comprising an admixture of the antisense molecule and an effective amount of a block copolymer. An example of this method is described in US patent application US 20040248833.

20 Other methods of delivery of antisense molecules to the nucleus are described in Mann CJ *et al.*, (2001) [*"Antisense-induced exon skipping and the synthesis of dystrophin in the mdx mouse"*]. Proc., Natl. Acad. Science, 98(1) 42-47J and in Gebiski *et al.*, (2003). Human Molecular Genetics, 12(15): 1801-1811.

25 A method for introducing a nucleic acid molecule into a cell by way of an expression vector either as naked DNA or complexed to lipid carriers, is described in US patent US 6,806,084.

It may be desirable to deliver the antisense molecule in a colloidal dispersion system. Colloidal dispersion systems include macromolecule complexes,

nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes or liposome formulations.

Liposomes are artificial membrane vesicles which are useful as delivery vehicles *in vitro* and *in vivo*. These formulations may have net cationic, anionic or neutral charge characteristics and are useful characteristics with *in vitro*, *in vivo* and *ex vivo* delivery methods. It has been shown that large unilamellar vesicles (LUV), which range in size from 0.2-4.0  $\mu$ m can encapsulate a substantial percentage of an aqueous buffer containing large macromolecules. RNA, and DNA can be encapsulated within the aqueous interior and be delivered to cells in a biologically active form (Fraley, *et al.*, Trends Biochem. Sci., 6:77, 1981).

In order for a liposome to be an efficient gene transfer vehicle, the following characteristics should be present: (1) encapsulation of the antisense molecule of interest at high efficiency while not compromising their biological activity; (2) preferential and substantial binding to a target cell in comparison to non-target cells; (3) delivery of the aqueous contents of the vesicle to the target cell cytoplasm at high efficiency; and (4) accurate and effective expression of genetic information (Mannino, *et al.*, Biotechniques, 6:682, 1988).

The composition of the liposome is usually a combination of phospholipids, particularly high-phase-transition-temperature phospholipids, usually in combination with steroids, especially cholesterol. Other phospholipids or other lipids may also be used. The physical characteristics of liposomes depend on pH, ionic strength, and the presence of divalent cations.

Alternatively, the antisense construct may be combined with other pharmaceutically acceptable carriers or diluents to produce a pharmaceutical composition. Suitable carriers and diluents include isotonic saline solutions, for example phosphate-buffered saline. The composition may be formulated for parenteral, intramuscular, intravenous, subcutaneous, intraocular, oral or transdermal administration.

The routes of administration described are intended only as a guide since a skilled practitioner will be able to determine readily the optimum route of administration

and any dosage for any particular animal and condition. Multiple approaches for introducing functional new genetic material into cells, both *in vitro* and *in vivo* have been attempted (Friedmann (1989) Science, 244:1275-1280).

These approaches include integration of the gene to be expressed into  
5 modified retroviruses (Friedmann (1989) *supra*; Rosenberg (1991) Cancer Research 51(18),  
suppl.: 5074S-5079S); integration into non-retrovirus vectors (Rosenfeld, *et al.* (1992) Cell,  
68:143-155; Rosenfeld, *et al.* (1991) Science, 252:431-434); or delivery of a transgene  
linked to a heterologous promoter-enhancer element via liposomes (Friedmann (1989),  
*supra*; Brigham, *et al.* (1989) Am. J. Med. Sci., 298:278-281; Nabel, *et al.* (1990) Science,  
10 249:1285-1288; Hazinski, *et al.* (1991) Am. J. Resp. Cell Molec. Biol., 4:206-209; and  
Wang and Huang (1987) Proc. Natl. Acad. Sci. (USA), 84:7851-7855); coupled to ligand-  
specific, cation-based transport systems (Wu and Wu (1988) J. Biol. Chem., 263:14621-  
14624) or the use of naked DNA, expression vectors (Nabel *et al.* (1990), *supra*); Wolff *et*  
*al.* (1990) Science, 247:1465-1468). Direct injection of transgenes into tissue produces  
15 only localized expression (Rosenfeld (1992) *supra*); Rosenfeld *et al.* (1991) *supra*; Brigham  
*et al.* (1989) *supra*; Nabel (1990) *supra*; and Hazinski *et al.* (1991) *supra*). The Brigham *et*  
*al.* group (Am. J. Med. Sci. (1989) 298:278-281 and Clinical Research (1991) 39  
(abstract)) have reported *in vivo* transfection only of lungs of mice following either  
intravenous or intratracheal administration of a DNA liposome complex. An example of a  
20 review article of human gene therapy procedures is: Anderson, Science (1992) 256:808-  
813.

The antisense molecules of the invention encompass any pharmaceutically  
acceptable salts, esters, or salts of such esters, or any other compound which, upon  
administration to an animal including a human, is capable of providing (directly or  
25 indirectly) the biologically active metabolite or residue thereof. Accordingly, for example,  
the disclosure is also drawn to prodrugs and pharmaceutically acceptable salts of the  
compounds of the invention, pharmaceutically acceptable salts of such pro-drugs, and other  
bioequivalents.



The term "pharmaceutically acceptable salts" refers to physiologically and pharmaceutically acceptable salts of the compounds of the invention: *i.e.*, salts that retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

5 For oligonucleotides, preferred examples of pharmaceutically acceptable salts include but are not limited to (a) salts formed with cations such as sodium, potassium, ammonium, magnesium, calcium, polyamines such as spermine and spermidine, etc.; (b) acid addition salts formed with inorganic acids, for example hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid and the like; (c) salts formed  
10 with organic acids such as, for example, acetic acid, oxalic acid, tartaric acid, succinic acid, malefic acid, fumaric acid, gluconic acid, citric acid, malic acid, ascorbic acid, benzoic acid, tannic acid, palmitic acid, alginic acid, polyglutamic acid, naphthalenesulfonic acid, methanesulfonic acid, p-toluenesulfonic acid, naphthalenedisulfonic acid, polygalacturonic acid, and the like; and (d) salts formed from elemental anions such as chlorine, bromine,  
15 and iodine. The pharmaceutical compositions of the present invention may be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic and to mucous membranes including rectal delivery), pulmonary, *e.g.*, by inhalation or insufflation of powders or aerosols, (including by nebulizer, intratracheal,  
20 intranasal, epidermal and transdermal), oral or parenteral. Parenteral administration includes intravenous, intra-arterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; or intracranial, *e.g.*, intrathecal or intraventricular, administration. Oligonucleotides with at least one 2'-O-methoxyethyl modification are believed to be particularly useful for oral administration.

25 The pharmaceutical formulations of the present invention, which may conveniently be presented in unit dosage form, may be prepared according to conventional techniques well known in the pharmaceutical industry. Such techniques include the step of bringing into association the active ingredients with the pharmaceutical carrier(s) or excipient(s). In general the formulations are prepared by uniformly and intimately bringing

into association the active ingredients with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

#### Kits of the Invention

5 The invention also provides kits for treatment of a patient with a genetic disease which kit comprises at least an antisense molecule, packaged in a suitable container, together with instructions for its use.

In a preferred embodiment, the kits will contain at least one antisense molecule as shown in Table 1A, or a cocktail of antisense molecules as shown in Table 1B or a "weasel" compound as shown in Table 1C. The kits may also contain peripheral  
10 reagents such as buffers, stabilizers, etc.

Those of ordinary skill in the field should appreciate that applications of the above method has wide application for identifying antisense molecules suitable for use in the treatment of many other diseases.

#### EXAMPLES

15 The following Examples serve to more fully describe the manner of using the above-described invention, as well as to set forth the best modes contemplated for carrying out various aspects of the invention. It is understood that these Examples in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. The references cited herein are expressly incorporated by reference.

20 Methods of molecular cloning, immunology and protein chemistry, which are not explicitly described in the following examples, are reported in the literature and are known by those skilled in the art. General texts that described conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art, included, for example: Sambrook *et al*, *Molecular Cloning: A Laboratory Manual*, Second  
25 Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York (1989); Glover ed., *DNA Cloning: A Practical Approach*, Volumes I and II, MRL Press, Ltd., Oxford, U.K. (1985); and Ausubel, F., Brent, R., Kingston, R.E., Moore, D.D., Seidman,

J.G., Smith, J.A., Struhl, K. *Current Protocols in Molecular Biology*. Greene Publishing Associates/Wiley Intersciences, New York (2002).

#### DETERMINING INDUCED EXON SKIPPING IN HUMAN MUSCLE CELLS

Attempts by the inventors to develop a rational approach in antisense molecules design were not completely successful as there did not appear to be a consistent trend that could be applied to all exons. As such, the identification of the most effective and therefore most therapeutic antisense molecules compounds has been the result of empirical studies.

These empirical studies involved the use of computer programs to identify motifs potentially involved in the splicing process. Other computer programs were also used to identify regions of the pre-mRNA which may not have had extensive secondary structure and therefore potential sites for annealing of antisense molecules. Neither of these approaches proved completely reliable in designing antisense oligonucleotides for reliable and efficient induction of exon skipping.

Annealing sites on the human dystrophin pre-mRNA were selected for examination, initially based upon known or predicted motifs or regions involved in splicing. 2OMe antisense oligonucleotides were designed to be complementary to the target sequences under investigation and were synthesised on an Expedite 8909 Nucleic Acid Synthesiser. Upon completion of synthesis, the oligonucleotides were cleaved from the support column and de-protected in ammonium hydroxide before being desalted. The quality of the oligonucleotide synthesis was monitored by the intensity of the trityl signals upon each deprotection step during the synthesis as detected in the synthesis log. The concentration of the antisense oligonucleotide was estimated by measuring the absorbance of a diluted aliquot at 260nm.

Specified amounts of the antisense molecules were then tested for their ability to induce exon skipping in an *in vitro* assay, as described below.

Briefly, normal primary myoblast cultures were prepared from human muscle biopsies obtained after informed consent. The cells were propagated and allowed

to differentiate into myotubes using standard culturing techniques. The cells were then transfected with the antisense oligonucleotides by delivery of the oligonucleotides to the cells as cationic lipoplexes, mixtures of antisense molecules or cationic liposome preparations.

5                   The cells were then allowed to grow for another 24 hours, after which total RNA was extracted and molecular analysis commenced. Reverse transcriptase amplification (RT-PCR) was undertaken to study the targeted regions of the dystrophin pre-mRNA or induced exonic re-arrangements.

10                   For example, in the testing of an antisense molecule for inducing exon 19 skipping the RT-PCR test scanned several exons to detect involvement of any adjacent exons. For example, when inducing skipping of exon 19, RT-PCR was carried out with primers that amplified across exons 17 and 21. Amplifications of even larger products in this area (*i.e.* exons 13-26) were also carried out to ensure that there was minimal amplification bias for the shorter induced skipped transcript. Shorter or exon skipped  
15 products tend to be amplified more efficiently and may bias the estimated of the normal and induced transcript.

                  The sizes of the amplification reaction products were estimated on an agarose gel and compared against appropriate size standards. The final confirmation of identity of these products was carried out by direct DNA sequencing to establish that the  
20 correct or expected exon junctions have been maintained.

                  Once efficient exon skipping had been induced with one antisense molecule, subsequent overlapping antisense molecules may be synthesized and then evaluated in the assay as described above. Our definition of an efficient antisense molecule is one that induces strong and sustained exon skipping at transfection concentrations in the order of  
25 300 nM or less.

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 8

Antisense oligonucleotides directed at exon 8 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5                Figure 3 shows differing efficiencies of two antisense molecules directed at exon 8 acceptor splice site. H8A(-06+18) [SEQ ID NO:1], which anneals to the last 6 bases of intron 7 and the first 18 bases of exon 8, induces substantial exon 8 and 9 skipping when delivered into cells at a concentration of 20 nM. The shorter antisense molecule, H8A(-06+14) [SEQ ID NO: 4] was only able to induce exon 8 and 9 skipping at 300 nM, a  
10                concentration some 15 fold higher than H8A(-06+18), which is the preferred antisense molecule.

                 This data shows that some particular antisense molecules induce efficient exon skipping while another antisense molecule, which targets a near-by or overlapping region, can be much less efficient. Titration studies show one compound is able to induce  
15                targeted exon skipping at 20 nM while the less efficient antisense molecules only induced exon skipping at concentrations of 300 nM and above. Therefore, we have shown that targeting of the antisense molecules to motifs involved in the splicing process plays a crucial role in the overall efficacy of that compound.

                 Efficacy refers to the ability to induce consistent skipping of a target exon.  
20                However, sometimes skipping of the target exons is consistently associated with a flanking exon. That is, we have found that the splicing of some exons is tightly linked. For example, in targeting exon 23 in the mouse model of muscular dystrophy with antisense molecules directed at the donor site of that exon, dystrophin transcripts missing exons 22 and 23 are frequently detected. As another example, when using an antisense molecule  
25                directed to exon 8 of the human dystrophin gene, all induced transcripts are missing both exons 8 and 9. Dystrophin transcripts missing only exon 8 are not observed.

                 Table 2 below discloses antisense molecule sequences that induce exon 8 (and 9) skipping.



SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
1	H8A(-06+18)	5'-GAU AGG UGG UAU CAA CAU CUG UAA	Very strong to 20 nM
2	H8A (-03+18)	5'-GAU AGG UGG UAU CAA CAU CUG	Very strong skipping to 40nM
3	H8A(-07+18)	5'-GAU AGG UGG UAU CAA CAU CUG UAA G	Strong skipping to 40nM
4	H8A(-06+14)	5'-GGU GGU AUC AAC AUC UGU AA	Skipping to 300nM
5	H8A(-10+10)	5'-GUA UCA ACA UCU GUA AGC AC	Patchy/weak skipping to 100nm

Table 2

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 7

Antisense oligonucleotides directed at exon 7 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

Figure 4 shows the preferred antisense molecule, H7A(+45+67) [SEQ ID NO: 6], and another antisense molecule, H7A(+2+26) [SEQ ID NO: 7], inducing exon 7 skipping. Nested amplification products span exons 3 to 9. Additional products above the induced transcript missing exon 7 arise from amplification from carry-over outer primers

10 from the RT-PCR as well as heteroduplex formation.

Table 3 below discloses antisense molecule sequences for induced exon 7 skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
6	H7A(+45+67)	5' - UGC AUG UUC CAG UCG UUG UGU GG	Strong skipping to 20nM
7	H7A(+02+26)	5' - CAC UAU UCC AGU CAA AUA GGU CUG G	Weak skipping at 100nM
8	H7D(+15-10)	5' -AUU UAC CAA CCU UCA GGA UCG AGU A	Weak skipping to 300nM
9	H7A(-18+03)	5' - GGC CUA AAA CAC AUA CAC AUA	Weak skipping to 300nM

Table 3

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 6

Antisense oligonucleotides directed at exon 6 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Figure 5 shows an example of two non-preferred antisense molecules inducing very low levels of exon 6 skipping in cultured human cells. Targeting this exon for specific removal was first undertaken during a study of the canine model using the oligonucleotides as listed in Table 4, below. Some of the human specific oligonucleotides were also evaluated, as shown in Figure 5. In this example, both antisense molecules target the donor splice site and only induced low levels of exon 6 skipping. Both H6D(+4-21) [SEQ ID NO: 17] and H6D(+18-4) [SEQ ID NO: 18] would be regarded as non-preferred antisense molecules.

One antisense oligonucleotide that induced very efficient exon 6 skipping in the canine model, C6A(+69+91) [SEQ ID NO: 14], would anneal perfectly to the corresponding region in human dystrophin exon 6. This compound was evaluated, found to be highly efficient at inducing skipping of that target exon, as shown in Figure 6 and is regarded as the preferred compound for induced exon 6 skipping. Table 4 below discloses antisense molecule sequences for induced exon 6 skipping.

SEQ ID	Antisense Oligo name	Sequence	Ability to induce skipping
10	C6A(-10+10)	5' CAU UUU UGA CCU ACA UGU GG	No skipping
11	C6A(-14+06)	5' UUU GAC CUA CAU GUG GAA AG	No skipping
12	C6A(-14+12)	5' UAC AUU UUU GAC CUA CAU GUG GAA AG	No skipping
13	C6A(-13+09)	5' AUU UUU GAC CUA CAU GGG AAA G	No skipping
14	CH6A(+69+91)	5' UAC GAG UUG AUU GUC GGA CCC AG	Strong skipping to 20 nM
15	C6D(+12-13)	5' GUG GUC UCC UUA CCU AUG ACU GUG G	Weak skipping at 300 nM
16	C6D(+06-11)	5' GGU CUC CUU ACC UAU GA	No skipping
17	H6D(+04-21)	5' UGU CUC AGU AAU CUU CUU ACC UAU	Weak skipping to 50 nM
18	H6D(+18-04)	5' UCU UAC CUA UGA CUA UGG AUG AGA	Very weak skipping to 300 nM

Table 4

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 4

Antisense oligonucleotides directed at exon 4 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

Figure 7 shows an example of a preferred antisense molecule inducing skipping of exon 4 skipping in cultured human cells. In this example, one preferred antisense compound, H4A(+13+32) [SEQ ID NO:19], which targeted a presumed exonic splicing enhancer induced efficient exon skipping at a concentration of 20 nM while other

10 non-preferred antisense oligonucleotides failed to induce even low levels of exon 4 skipping. Another preferred antisense molecule inducing skipping of exon 4 was H4A(+111+40) [SEQ ID NO:22], which induced efficient exon skipping at a concentration of 20 nM.

Table 5 below discloses antisense molecule sequences for inducing exon 4

15 skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
19	H4A(+13+32)	5' GCA UGA ACU CUU GUG GAU CC	Skipping to 20 nM
22	H4A(+11+40)	5' UGU UCA GGG CAU GAA CUC UUG UGG AUC CUU	Skipping to 20 nM
20	H4D(+04-16)	5' CCA GGG UAC UAC UUA CAU UA	No skipping
21	H4D(-24-44)	5' AUC GUG UGU CAC AGC AUC CAG	No skipping

Table 5

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 3

Antisense oligonucleotides directed at exon 3 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H3A(+30+60) [SEQ ID NO:23] induced substantial exon 3 skipping when delivered into cells at a concentration of 20 nM to 600 nM. The antisense molecule, H3A(+35+65) [SEQ ID NO: 24] induced exon skipping at 300 nM.

Table 6 below discloses antisense molecule sequences that induce exon 3  
10 skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
23	H3A(+30+60)	UAG GAG GCG CCU CCC AUC CUG UAG GUC ACU G	Moderate skipping to 20 to 600 nM
24	H3A(+35+65)	AGG UCU AGG AGG CGC CUC CCA UCC UGU AGG U	Working to 300 nM
25	H3A(+30+54)	GCG CCU CCC AUC CUG UAG GUC ACU G	Moderate 100-600 nM
26	H3D(+46-21)	CUU CGA GGA GGU CUA GGA GGC GCC UC	No skipping
27	H3A(+30+50)	CUC CCA UCC UGU AGG UCA CUG	Moderate 20-600 nM
28	H3D(+19-03)	UAC CAG UUU UUG CCC UGU CAG G	No skipping
29	H3A(-06+20)	UCA AUA UGC UGC UUCCCA AAC UGA AA	No skipping

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
30	H3A(+37+61)	CUA GGA GGC GCC UCC CAU CCU GUA G	No skipping

Table 6

# ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 5

Antisense oligonucleotides directed at exon 5 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H5A(+20+50) [SEQ ID NO:31] induces substantial exon 5 skipping when delivered into cells at a concentration of 100 nM. Table 7 below shows other antisense molecules tested. The majority of these antisense molecules were not as effective at exon skipping as H5A(+20+50). However, H5A(+15+45) [SEQ ID NO: 40] was able to induce

10 exon 5 skipping at 300 nM.

Table 7 below discloses antisense molecule sequences that induce exon 5 skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
31	H5A(+20+50)	UUA UGA UUU CCA UCU ACG AUG UCA GUA CUU C	Working to 100 nM
32	H5D(+25-05)	CUU ACC UGC CAG UGG AGG AUU AUA UUC CAA A	No skipping
33	H5D(+10-15)	CAU CAG GAU UCU UAC CUG CCA GUG G	Inconsistent at 300 nM
34	H5A(+10+34)	CGA UGU CAG UAC UUC CAA UAU UCA C	Very weak
35	H5D(-04-21)	ACC AUU CAU CAG GAU UCU	No skipping
36	H5D(+16-02)	ACC UGC CAG UGG AGG AUU	No skipping
37	H5A(-07+20)	CCA AUA UUC ACU AAA UCA ACC UGU UAA	No skipping
38	H5D(+18-12)	CAG GAU UCU UAC CUG CCA GUG GAG GAU UAU	No skipping



SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
39	H5A(+05+35)	ACG AUG UCA GUA CUU CCA AUA UUC ACU AAA U	No skipping
40	H5A(+15+45)	AUU UCC AUC UAC GAU GUC AGU ACU UCC AAU A	Working to 300 nM

Table 7

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 10

Antisense oligonucleotides directed at exon 10 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H10A(-05+16) [SEQ ID NO:41] induced substantial exon 10 skipping when delivered into cells. Table 8 below shows other antisense molecules tested. The antisense molecules ability to induce exon skipping was variable. Table 8 below discloses antisense molecule sequences that induce exon 10 skipping.

10

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
41	H10A(-05+16)	CAG GAG CUU CCA AAU GCU GCA	Not tested
42	H10A(-05+24)	CUU GUC UUC AGG AGC UUC CAA AUG CUG CA	Not tested
43	H10A(+98+119)	UCC UCA GCA GAA AGA AGC CAC G	Not tested
44	H10A(+130+149)	UUA GAA AUC UCU CCU UGU GC	No skipping
45	H10A(-33-14)	UAA AUU GGG UGU UAC ACA AU	No skipping

Table 8

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 11

Antisense oligonucleotides directed at exon 11 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

15 described above.

Figure 8B shows an example of H11A(+75+97) [SEQ ID NO:49] antisense molecule inducing exon 11 skipping in cultured human cells. H11A(+75+97) induced substantial exon 11 skipping when delivered into cells at a concentration of 5 nM. Table 9

below shows other antisense molecules tested. The antisense molecules ability to induce exon skipping was observed at 100 nM.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
46	H11D(+26+49)	CCC UGA GGC AUU CCC AUC UUG AAU	Skipping at 100 nM
47	H11D(+11-09)	AGG ACU UAC UUG CUU UGU UU	Skipping at 100 nM
48	H11A(+118+140)	CUU GAA UUU AGG AGA UUC AUC UG	Skipping at 100 nM
49	H11A(+75+97)	CAU CUU CUG AUA AUU UUC CUG UU	Skipping at 100 nM
46	H11D(+26+49)	CCC UGA GGC AUU CCC AUC UUG AAU	Skipping at 5nM

Table 9

## 5 ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 12

Antisense oligonucleotides directed at exon 12 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

H12A(+52+75) [SEQ ID NO:50] induced substantial exon 12 skipping when delivered into cells at a concentration of 5 nM, as shown in Figure 8A. Table 10 below shows other antisense molecules tested at a concentration range of 5, 25, 50, 100, 200 and 300 nM. The antisense molecules ability to induce exon skipping was variable.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
50	H12A(+52+75)	UCU UCU GUU UUU GUU AGC CAG UCA	Skipping at 5 nM
51	H12A(-10+10)	UCU AUG UAA ACU GAA AAU UU	Skipping at 100 nM
52	H12A(+11+30)	UUC UGG AGA UCC AUU AAA AC	No skipping

Table 10

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 13

Antisense oligonucleotides directed at exon 13 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5 H13A(+77+100) [SEQ ID NO:53] induced substantial exon 13 skipping when delivered into cells at a concentration of 5 nM. Table 11 below includes two other antisense molecules tested at a concentration range of 5, 25, 50, 100, 200 and 300 nM. These other antisense molecules were unable to induce exon skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
53	H13A(+77+100)	CAG CAG UUG CGU GAU CUC CAC UAG	Skipping at 5 nM
54	H13A(+55+75)	UUC AUC AAC UAC CAC CAC CAU	No skipping
55	H13D(+06-19)	CUA AGC AAA AUA AUC UGA CCU UAA G	No skipping

10 Table 11

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 14

Antisense oligonucleotides directed at exon 14 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

15 H14A(+37+64) [SEQ ID NO:56] induced weak exon 14 skipping when delivered into cells at a concentration of 100 nM. Table 12 below includes other antisense molecules tested at a concentration range of 5, 25, 50, 100, 200 and 300 nM. The other antisense molecules were unable to induce exon skipping at any of the concentrations tested.

20

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
56	H14A(+37+64)	CUU GUA AAA GAA CCC AGC GGU CUU CUG U	Skipping at 100 nM

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
57	H14A(+14+35)	CAU CUA CAG AUG UUU GCC CAU C	No skipping
58	H14A(+51+73)	GAA GGA UGU CUU GUA AAA GAA CC	No skipping
59	H14D(-02+18)	ACC UGU UCU UCA GUA AGA CG	No skipping
60	H14D(+14-10)	CAU GAC ACA CCU GUU CUU CAG UAA	No skipping
61	H14A(+61 +80)	CAU UUG AGA AGG AUG UCU UG	No skipping
62	H14A(-12+12)	AUC UCC CAA UAC CUG GAG AAG AGA	No skipping

Table 12

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 15

Antisense oligonucleotides directed at exon 15 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H15A(-12+19) [SEQ ID NO:63] and H15A(+48+71) [SEQ ID NO:64] induced substantial exon 15 skipping when delivered into cells at a concentration of 10 Nm, as shown in Figure 9A. Table 13 below includes other antisense molecules tested at a concentration range of 5, 25, 50, 100, 200 and 300 Nm. These other antisense molecules

10 were unable to induce exon skipping at any of the concentrations tested.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
63	H15A(-12+19)	GCC AUG CAC UAA AAA GGC ACU GCA AGA CAU U	Skipping at 5Nm
64	H15A(+48+71)	UCU UUA AAG CCA GUU GUG UGA AUC	Skipping at 5Nm
65	H15A(+08+28)	UUU CUG AAA GCC AUG CAC UAA	No skipping
63	H15A(-12+19)	GCC AUG CAC UAA AAA GGC ACU GCA AGA CAU U	No skipping
66	H15D(+17-08)	GUA CAU ACG GCC AGU UUU UGA AGA C	No skipping

Table 13

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 16

Antisense oligonucleotides directed at exon 16 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H16A(-12+19) [SEQ ID NO:67] and H16A(-06+25) [SEQ ID NO:68] induced substantial exon 16 skipping when delivered into cells at a concentration of 10 nM, as shown in Figure 9B. Table 14 below includes other antisense molecules tested. H16A(-06+19) [SEQ ID NO:69] and H16A(+87+109) [SEQ ID NO:70] were tested at a  
10 concentration range of 5, 25, 50, 100, 200 and 300 nM. These two antisense molecules were able to induce exon skipping at 25 nM and 100 nM, respectively. Additional antisense molecules were tested at 100, 200 and 300 nM and did not result in any exon skipping.

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
67	H16A(-12+19)	CUA GAU CCG CUU UUA AAA CCU GUU AAA ACA A	Skipping at 5 nM
68	H16A(-06+25)	UCU UUU CUA GAU CCG CUU UUA AAA CCU GUU A	Skipping at 5 nM
69	H16A(-06+19)	CUA GAU CCG CUU UUA AAA CCU GUU A	Skipping at 25 nM
70	H16A(+87+109)	CCG UCU UCU GGG UCA CUG ACU UA	Skipping at 100 nM



SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
71	H16A(-07+19)	CUA GAU CCG CUU UUA AAA CCU GUU AA	No skipping
72	H16A(-07+13)	CCG CUU UUA AAA CCU GUU AA	No skipping
73	H16A(+12+37)	UGG AUU GCU UUU UCU UUU CUA GAU CC	No skipping
74	H16A(+92+116)	CAU GCU UCC GUC UUC UGG GUC ACU G	No skipping
75	H16A(+45+67)	G AUC UUG UUU GAG UGA AUA CAG U	No skipping
76	H16A(+105+126)	GUU AUC CAG CCA UGC UUC CGU C	No skipping
77	H16D(+05-20)	UGA UAA UUG GUA UCA CUA ACC UGU G	No skipping
78	H16D(+12-11)	GUA UCA CUA ACC UGU GCU GUA C	No skipping

Table 14

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 19

Antisense oligonucleotides directed at exon 19 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H19A(+35+65) [SEQ ID NO:79] induced substantial exon 19 skipping when delivered into cells at a concentration of 10 nM. This antisense molecule also showed very strong exon skipping at concentrations of 25, 50, 100, 300 and 600 nM.

Figure 10 illustrates exon 19 and 20 skipping using a "cocktail" of antisense  
10 oligonucleotides, as tested using gel electrophoresis. It is interesting to note that it was not easy to induce exon 20 skipping using single antisense oligonucleotides H20A(+44+71) [SEQ ID NO:81] or H20A(+149+170) [SEQ ID NO:82], as illustrated in sections 2 and 3 of the gel shown in Figure 10. Whereas, a "cocktail" of antisense oligonucleotides was more efficient as can be seen in section 4 of Figure 10 using a "cocktail" of antisense  
15 oligonucleotides H20A(+44+71) and H20A(+149+170). When the cocktail was used to target exon 19, skipping was even stronger (see section 5, Figure 10).

Figure 11 illustrates gel electrophoresis results of exon 19/20 skipping using "weasels" The "weasels" were effective in skipping exons 19 and 20 at concentrations of 25, 50, 100, 300 and 600 nM. A further "weasel" sequence is shown in the last row of  
20 Table 3C. This compound should give good results.

# ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 20

Antisense oligonucleotides directed at exon 20 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5 None of the antisense oligonucleotides tested induced exon 20 skipping when delivered into cells at a concentration of 10, 25, 50, 300 or 600 nM (see Table 15). Antisense molecules H20A(-11+17) [SEQ ID NO:86] and H20D(+08-20) [SEQ ID NO:87] are yet to be tested.

10 However, a combination or "cocktail" of H20A(+44+71) [SEQ ID NO: 81] and H20(+149+170) [SEQ ID NO:82] in a ratio of 1:1, exhibited very strong exon skipping at a concentration of 100 nM and 600 nM. Further, a combination of antisense molecules H19A(+35+65) [SEQ ID NO:79], H20A(+44+71) [SEQ ID NO:81] and H20A(+149+170) [SEQ ID NO:82] in a ratio of 2:1:1, induced very strong exon skipping at a concentration ranging from 10 nM to 600 nM.

15

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
81	H20A(+44+71)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C	No skipping
82	H20A(+147+168)	CAG CAG UAG UUG UCA UCU GCU C	No skipping
83	H20A(+185+203)	UGA UGG GGU GGU GGG UUG G	No skipping
84	H20A(-08+17)	AUC UGC AUU AAC ACC CUC UAG AAA G	No skipping
85	H20A(+30+53)	CCG GCU GUU CAG UUG UUC UGA GGC	No skipping
86	H20A(-11+17)	AUC UGC AUU AAC ACC CUC UAG AAA GAA A	Not tested yet
87	H20D(+08-20)	GAA GGA GAA GAG AUU CUU ACC UUA CAA A	Not tested yet
81 & 82	H20A(+44+71) & H20A(+147+168)	CUG GCA GAA UUC GAU CCA CCG GCU GUU C CAG CAG UAG UUG UCA UCU GCU C	Very strong skipping
80, 81	H19A(+35+65);	GCC UGA GCU GAU CUG CUG GCA UCU	Very strong

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
& 82	H20A(+44+71); H20A(+147+168)	UGC AGU U; CUG GCA GAA UUC GAU CCA CCG GCU GUU C; CAG CAG UAG UUG UCA UCU GCU C	skipping

Table 15

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 21

Antisense oligonucleotides directed at exon 21 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

H21A(+85+108) [SEQ ID NO:92] and H21A(+85+106) [SEQ ID NO:91] induced exon 21 skipping when delivered into cells at a concentration of 50 nM. Table 16 below includes other antisense molecules tested at a concentration range of 5, 25, 50, 100, 200 and 300 nM. These antisense molecules showed a variable ability to induce exon

10 skipping

SEQ ID	Antisense Oligonucleotide name	Sequence	Ability to induce skipping
90	H21A(-06+16)	GCC GGU UGA CUU CAU CCU GUG C	Skips at 600 nM
91	H21A(+85+106)	CUG CAU CCA GGA ACA UGG GUC C	Skips at 50 nM
92	H21A(+85+108)	GUC UGC AUC CAG GAA CAU GGG UC	Skips at 50 nM
93	H21A(+08+31)	GUU GAA GAU CUG AUA GCC GGU UGA	Skips faintly to
94	H21D(+18-07)	UAC UUA CUG UCU GUA GCU CUU UCU	No skipping

Table 16

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 22

Antisense oligonucleotides directed at exon 22 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

15 described above.

Figure 12 illustrates differing efficiencies of two antisense molecules directed at exon 22 acceptor splice site. H22A(+125+106) [SEQ ID NO:96] and H22A(+80+101) [SEQ ID NO: 98] induce strong exon 22 skipping from 50 nM to 600 nM concentration.

5 H22A(+125+146) [SEQ ID NO:96] and H22A(+80+101) [SEQ ID NO:98] induced exon 22 skipping when delivered into cells at a concentration of 50 nM. Table 17 below shows other antisense molecules tested at a concentration range of 50, 100, 300 and 600 nM. These antisense molecules showed a variable ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
95	H22A(+22+45)	CAC UCA UGG UCU CCU GAU AGC GCA	No skipping
96	H22A(+125+146)	CUG CAA UUC CCC GAG UCU CUG C	Skipping to 50 nM
97	H22A(+47+69)	ACU GCU GGA CCC AUG UCC UGA UG	Skipping to 300 nM
98	H22A(+80+101)	CUA AGU UGA GGU AUG GAG AGU	Skipping to 50 nM
99	H22D(+13-11)	UAU UCA CAG ACC UGC AAU UCC CC	No skipping

10 Table 17

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 23

Antisense oligonucleotides directed at exon 23 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

15 Table 18 below shows antisense molecules tested at a concentration range of 25, 50, 100, 300 and 600 nM. These antisense molecules showed no ability to induce exon skipping or are yet to be tested.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
100	H23A(+34+59)	ACA GUG GUG CUG AGA UAG UAU AGG CC	No skipping
101	H23A(+18+39)	UAG GCC ACU UUG UUG CUC UUG C	No Skipping
102	H23A(+72+90)	UUC AGA GGG CGC UUU CUU C	No Skipping

Table 18

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 24

Antisense oligonucleotides directed at exon 24 were prepared using similar methods as described above. Table 19 below outlines the antisense oligonucleotides 5 directed at exon 24 that are yet to be tested for their ability to induce exon 24 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
103	H24A(+48+70)	GGG CAG GCC AUU CCU CCU UCA GA	Needs testing
104	H24A(-02+22)	UCU UCA GGG UUU GUA UGU GAU UCU	Needs testing

Table 19

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 25

Antisense oligonucleotides directed at exon 25 were prepared using similar 10 methods as described above. Table 20 below shows the antisense oligonucleotides directed at exon 25 that are yet to be tested for their ability to induce exon 25 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
105	H25A(+9+36)	CUG GGC UGA AUU GUC UGA AUA UCA CUG	Needs testing
106	H25A(+131+156)	CUG UUG GCA CAU GUG AUC CCA CUG AG	Needs testing
107	H25D(+16-08)	GUC UAU ACC UGU UGG CAC AUG UGA	Needs testing

Table 20



### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 26

Antisense oligonucleotides directed at exon 26 were prepared using similar methods as described above. Table 21 below outlines the antisense oligonucleotides directed at exon 26 that are yet to be tested for their ability to induce exon 26 skipping.

5

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
108	H26A(+132+156)	UGC UUU CUG UAA UUC AUC UGG AGU U	Needs testing
109	H26A(-07+19)	CCU CCU UUC UGG CAU AGA CCU UCC AC	Needs testing
110	H26A(+68+92)	UGU GUC AUC CAU UCG UGC AUC UCU G	Faint skipping at 600 nM

Table 21

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 27

Antisense oligonucleotides directed at exon 27 were prepared using similar methods as described above. Table 22 below outlines the antisense oligonucleotides directed at exon 27 that are yet to be tested for their ability to induce exon 27 skipping.

10

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
111	H27A(+82+106)	UUA AGG CCU CUU GUG CUA CAG GUG G	Needs testing
112	H27A(-4+19)	GGG CCU CUU CUU UAG CUC UCU GA	Faint skipping at 600 and 300 nM
113	H27D(+19-03)	GAC UUC CAA AGU CUU GCA UUU C	v. strong skipping at 600 and 300 nM

Table 22

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 28

Antisense oligonucleotides directed at exon 28 were prepared using similar methods as described above. Table 23 below outlines the antisense oligonucleotides directed at exon 28 that are yet to be tested for their ability to induce exon 28 skipping.

15

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
114	H28A(-05+19)	GCC AAC AUG CCC AAA CUU CCU AAG	v. strong skipping at 600 and 300 nM
115	H28A(+99+124)	CAG AGA UUU CCU CAG CUC CGC CAG GA	Needs testing
116	H28D(+16-05)	CUU ACA UCU AGC ACC UCA GAG	v. strong skipping at 600 and 300 nM

Table 23

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 29

Antisense oligonucleotides directed at exon 29 were prepared using similar methods as described above. Table 24 below outlines the antisense oligonucleotides directed at exon 29 that are yet to be tested for their ability to induce exon 29 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
117	H29A(+57+81)	UCC GCC AUC UGU UAG GGU CUG UGC C	Needs testing
118	H29A(+18+42)	AUU UGG GUU AUC CUC UGA AUG UCG C	v. strong skipping at 600 and 300 nM
119	H29D(+17-05)	CAU ACC UCU UCA UGU AGU UCC C	v. strong skipping at 600 and 300 nM

Table 24

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 30

Antisense oligonucleotides directed at exon 30 were prepared using similar methods as described above. Table 25 below outlines the antisense oligonucleotides directed at exon 30 that are yet to be tested for their ability to induce exon 30 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
120	H30A(+122+147)	CAU UUG AGC UGC GUC CAC CUU GUC UG	Needs testing
121	H30A(+25+50)	UCC UGG GCA GAC UGG AUG CUC UGU UC	Very strong skipping at 600 and 300 nM.
122	H30D(+19-04)	UUG CCU GGG CUU CCU GAG GCA UU	Very strong skipping at 600 and 300 nM.

Table 25

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 31

Antisense oligonucleotides directed at exon 31 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as

5 described above.

Figure 13 illustrates differing efficiencies of two antisense molecules directed at exon 31 acceptor splice site and a "cocktail" of exon 31 antisense oligonucleotides at varying concentrations. H31D(+03-22) [SEQ ID NO:124] substantially induced exon 31 skipping when delivered into cells at a concentration of 20 nM. Table 26 below also includes other antisense molecules tested at a concentration of 100 and 300 nM. These antisense molecules showed a variable ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
123	H31D(+06-18)	UUC UGA AAU AAC AUA UAC CUG UGC	Skipping to 300 nM
124	H31D(+03-22)	UAG UUU CUG AAA UAA CAU AUA CCU G	Skipping to 20 nM
125	H31A(+05+25)	GAC UUG UCA AAU CAG AUU GGA	No skipping
126	H31D(+04-20)	GUU UCU GAA AUA ACA UAU ACC UGU	Skipping to 300 nM

Table 26

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 32

Antisense oligonucleotides directed at exon 32 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5 H32D(+04-16) [SEQ ID NO:127] and H32A(+49+73) [SEQ ID NO:130] induced exon 32 skipping when delivered into cells at a concentration of 300 nM. Table 27 below also shows other antisense molecules tested at a concentration of 100 and 300 nM. These antisense molecules did not show an ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
127	H32D(+04-16)	CAC CAG AAA UAC AUA CCA CA	Skipping to 300 nM
128	H32A(+151+170)	CAA UGA UUU AGC UGU GAC UG	No skipping
129	H32A(+10+32)	CGA AAC UUC AUG GAG ACA UCU UG	No skipping
130	H32A(+49+73)	CUU GUA GAC GCU GCU CAA AAU UGG C	Skipping to 300 nM

10 Table 27

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 33

Antisense oligonucleotides directed at exon 33 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

15 Figure 14 shows differing efficiencies of two antisense molecules directed at exon 33 acceptor splice site. H33A(+64+88) [SEQ ID NO:134] substantially induced exon 33 skipping when delivered into cells at a concentration of 10 nM. Table 28 below includes other antisense molecules tested at a concentration of 100, 200 and 300 nM. These antisense molecules showed a variable ability to induce exon skipping.

20

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
131	H33D(+09-11)	CAU GCA CAC ACC UUU GCU CC	No skipping
132	H33A(+53+76)	UCU GUA CAA UCU GAC GUC CAG UCU	Skipping to 200 nM
133	H33A(+30+56)	GUG UUU AUC ACC AUU UCC ACU UCA GAC	Skipping to 200 nM
134	H33A(+64+88)	GCG UCU GCU UUU UCU GUA CAA UCU G	Skipping to 10 nM

Table 28

ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 34

Antisense oligonucleotides directed at exon 34 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as 5 described above.

Table 29 below includes antisense molecules tested at a concentration of 100 and 300 nM. These antisense molecules showed a variable ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
135	H34A(+83+104)	UCC AUA UCU GUA GCU GGC AGC C	No skipping
136	H34A(+143+165)	CCA GGC AAC UUC AGA AUC CAA AU	No skipping
137	H34A(-20+10)	UUU CUG UUA CCU GAA AAG AAU UAU AAU GAA	Not tested
138	H34A(+46+70)	CAU UCA UUU CCU UUC GCA UCU UAC G	Skipping to 300 nM
139	H34A(+95+120)	UGA UCU CUU UGU CAA UUC CAU AUC UG	Skipping to 300 nM
140	H34D(+10-20)	UUC AGU GAU AUA GGU UUU ACC UUU CCC CAG	Not tested
141	H34A(+72+96)	CUG UAG CUG CCA GCC AUU CUG UCA AG	No skipping

Table 29

10



### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 35

Antisense oligonucleotides directed at exon 35 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5 Figure 15 shows differing efficiencies of antisense molecules directed at exon 35 acceptor splice site. H35A(+24+43) [SEQ ID NO:144] substantially induced exon 35 skipping when delivered into cells at a concentration of 20 nM. Table 30 below also includes other antisense molecules tested at a concentration of 100 and 300 nM. These antisense molecules showed no ability to induce exon skipping.

10

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
142	H35A(+141+161)	UCU UCU GCU CGG GAG GUG ACA	Skipping to 20 nM
143	H35A(+116+135)	CCA GUU ACU AUU CAG AAG AC	No skipping
144	H35A(+24+43)	UCU UCA GGU GCA CCU UCU GU	No skipping

Table 30

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 36

Antisense oligonucleotides directed at exon 36 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

15

Antisense molecule H36A(+26+50) [SEQ ID NO:145] induced exon 36 skipping when delivered into cells at a concentration of 300 nM, as shown in Figure 16.

### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 37

Antisense oligonucleotides directed at exon 37 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

20

Figure 17 shows differing efficiencies of two antisense molecules directed at exon 37 acceptor splice site. H37A(+82+105) [SEQ ID NO:148] and H37A(+134+157)

[SEQ ID NO:149] substantially induced exon 37 skipping when delivered into cells at a concentration of 10 nM. Table 31 below shows the antisense molecules tested.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
147	H37A(+26+50)	CGU GUA GAG UCC ACC UUU GGG CGU A	No skipping
148	H37A(+82+105)	UAC UAA UUU CCU GCA GUG GUC ACC	Skipping to 10 nM
149	H37A(+134+157)	UUC UGU GUG AAA UGG CUG CAA AUC	Skipping to 10 nM

Table 31

## 5 ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 38

Antisense oligonucleotides directed at exon 38 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Figure 18 illustrates antisense molecule H38A(+88+112) [SEQ ID NO:152], directed at exon 38 acceptor splice site. H38A(+88+112) substantially induced exon 38 skipping when delivered into cells at a concentration of 10 nM. Table 32 below shows the antisense molecules tested and their ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
150	H38A(-01+19)	CCU UCA AAG GAA UGG AGG CC	No skipping
151	H38A(+59+83)	UGC UGA AUU UCA GCC UCC AGU GGU U	Skipping to 10 nM
152	H38A(+88+112)	UGA AGU CUU CCU CUU UCA GAU UCA C	Skipping to 10 nM

Table 32

## 15 ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 39

Antisense oligonucleotides directed at exon 39 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

H39A(+62+85) [SEQ ID NO:153] induced exon 39 skipping when delivered into cells at a concentration of 100 nM. Table 33 below shows the antisense molecules tested and their ability to induce exon skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
153	H39A(+62+85)	CUG GCU UUC UCU CAU CUG UGA UUC	Skipping to 100 nM
154	H39A(+39+58)	GUU GUA AGU UGU CUC CUC UU	No skipping
155	H39A(+102+121)	UUG UCU GUA ACA GCU GCU GU	No skipping
156	H39D(+10-10)	GCU CUA AUA CCU UGA GAG CA	Skipping to 300 nM

5 Table 33

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 40

Antisense oligonucleotides directed at exon 40 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

10 Figure 19 illustrates antisense molecule H40A(-05+17) [SEQ ID NO:157] directed at exon 40 acceptor splice site. H40A(-05+17) and H40A(+129+153) [SEQ ID NO:158] both substantially induced exon 40 skipping when delivered into cells at a concentration of 5 nM.

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 42

15 Antisense oligonucleotides directed at exon 42 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Figure 20 illustrates antisense molecule H42A(-04+23) [SEQ ID NO:159], directed at exon 42 acceptor splice site. H42A(-4+23) and H42D(+19-02) [SEQ ID NO:161] both induced exon 42 skipping when delivered into cells at a concentration of 5 nM. Table 34 below shows the antisense molecules tested and their ability to induce exon 42 skipping.

SEQ ID	Antisense afigonucleotide name	Sequence	Ability to induce skipping
159	H42A(-4+23)	AUC GUU UCU UCA CGG ACA GUG UGG UGC	Skipping to 5 nM
160	H42A(+86+109)	GGG CUU GUG AGA CAU GAG UGA UUU	Skipping to 100 nM
161	H42D(+19-02)	A CCU UCA GAG GAC UCC UCU UGC	Skipping to 5 nM

Table 34

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 43

Antisense oligonucleotides directed at exon 43 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

H43A(+101+120) [SEQ ID NO:163] induced exon 43 skipping when delivered into cells at a concentration of 25 nM. Table 35 below includes the antisense molecules tested and their ability to induce exon 43 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
162	H43D(+10-15)	UAU GUG UUA CCU ACC CUU GUC GGU C	Skipping to 100 nM
163	H43A(+101+120)	GGA GAG AGC UUC CUG UAG CU	Skipping to 25 nM
164	H43A(+78+100)	UCA CCC UUU CCA CAG GCG UUG CA	Skipping to 200 nM

Table 35

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 44

Antisense oligonucleotides directed at exon 44 were prepared using similar methods as described above. Testing for the ability of these antisense molecules to induce exon 44 skipping is still in progress. The antisense molecules under review are shown as SEQ ID Nos: 165 to 167 in Table 1A.

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 45

Antisense oligonucleotides directed at exon 45 were prepared using similar methods as described above. Testing for the ability of these antisense molecules to induce exon 45 skipping is still in progress. The antisense molecules under review are shown as

5 SEQ ID Nos: 207 to 211 in Table 1A.

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 46

Antisense oligonucleotides directed at exon 46 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

10 Figure 21 illustrates the efficiency of one antisense molecule directed at exon 46 acceptor splice site. Antisense oligonucleotide H46A(+86+115) [SEQ ID NO:203] showed very strong ability to induce exon 46 skipping. Table 36 below includes antisense molecules tested. These antisense molecules showed varying ability to induce exon 46 skipping.

15

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
168	H46D(+16-04)	UUA CCU UGA CUU GCU CAA GC	No skipping
169	H46A(+90+109)	UCC AGG UUC AAG UGG GAU AC	No skipping
203	H46A(+86+115)	CUC UUU UCC AGG UUC AAG UGG GAU ACU AGC	Good skipping to 100 nM
204	H46A(+107+137)	CAA GCU UUU CUU UUA GUU GCU GCU CUU UUC C	Good skipping to 100 nM
205	H46A(-10+20)	UAU UCU UUU GUU CUU CUA GCC UGG AGA AAG	Weak skipping
206	H46A(+50+77)	CUG CUU CCU CCA ACC AUA AAA CAA AUU C	Weak skipping

Table 36



ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 47

Antisense oligonucleotides directed at exon 47 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

5 H47A(+76+100) [SEQ ID NO:170] and H47A(-09+12) [SEQ ID NO:172] both induced exon 47 skipping when delivered into cells at a concentration of 200 nM. H47D(+25-02) [SEQ ID NO: 171] is yet to be prepared and tested.

ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 50

10 Antisense oligonucleotides directed at exon 50 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Antisense oligonucleotide molecule H50A(+02+30) [SEQ ID NO: 173] was a strong inducer of exon skipping. Further, H50A(+07+33) [SEQ ID NO:174] and H50D(+07-18) [SEQ ID NO:175] both induced exon 50 skipping when delivered into cells  
15 at a concentration of 100 nM.

ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 51

Antisense oligonucleotides directed at exon 51 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

20 Figure 22 illustrates differing efficiencies of two antisense molecules directed at exon 51 acceptor splice site. Antisense oligonucleotide H51A(+66+90) [SEQ ID NO:180] showed the stronger ability to induce exon 51 skipping. Table 37 below includes antisense molecules tested at a concentration range of 25, 50, 100, 300 and 600 nM. These antisense molecules showed varying ability to induce exon 51 skipping. The  
25 strongest inducers of exon skipping were antisense oligonucleotide H51A(+61+90) [SEQ ID NO: 179] and H51A(+66+95) [SEQ ID NO: 181].

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
176	H51A(-01+25)	ACC AGA GUA ACA GUC UGA GUA GGA GC	Faint skipping
177	H51D(+16-07)	CUC AUA CCU UCU GCU UGA UGA UC	Skipping at 300 nM
178	H51A(+111+134)	UUC UGU CCA AGC CCG GUU GAA AUC	Needs re- testing
179	H51A(+61+90)	ACA UCA AGG AAG AUG GCA UUU CUA GUU UGG	Very strong skipping
180	H51A(+66+90)	ACA UCA AGG AAG AUG GCA UUU CUA G	skipping
181	H51A(+66+95)	CUC CAA CAU CAA GGA AGA UGG CAU UUC UAG	Very strong skipping
182	H51D(+08-17)	AUC AUU UUU UCU CAU ACC UUC UGC U	No skipping
183	H51A/D(+08-17) & (-15+?)	AUC AUU UUU UCU CAU ACC UUC UGC UAG GAG CUA AAA	No skipping
184	H51A(+175+195)	CAC CCA CCA UCA GCC UCU GUG	No skipping
185	H51A(+199+220)	AUC AUC UCG UUG AUA UCC UCA A	No skipping

Table 37

#### ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 52

Antisense oligonucleotides directed at exon 52 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Figure 22 also shows differing efficiencies of four antisense molecules directed at exon 52 acceptor splice site. The most effective antisense oligonucleotide for inducing exon 52 skipping was H52A(+17+37) [SEQ ID NO:188].

Table 38 below shows antisense molecules tested at a concentration range of 50, 100, 300 and 600 nM. These antisense molecules showed varying ability to induce exon 50 skipping. Antisense molecules H52A(+12+41) [SEQ ID NO:187] and

H52A(+17+37) [SEQ ID NO:188] showed the strongest exon 50 skipping at a concentration of 50 nM.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
186	H52A(-07+14)	UCC UGC AUU GUU GCC UGU AAG	No skipping
187	H52A(+12+41)	UCC AAC UGG GGA CGC CUC UGU UCC AAA UCC	Very strong skipping
188	H52A(+17+37)	ACU GGG GAC GCC UCU GUU CCA	Skipping to 50 nM
189	H52A(+93+112)	CCG UAA UGA UUG UUC UAG CC	No skipping
190	H52D(+05-15)	UGU UAA AAA ACU UAC UUC GA	No skipping

Table 38

## 5 ANTISENSE OLIGONUCLEOTIDES DIRECTED AT EXON 53

Antisense oligonucleotides directed at exon 53 were prepared and tested for their ability to induce exon skipping in human muscle cells using similar methods as described above.

Figure 22 also shows antisense molecule H53A(+39+69) [SEQ ID NO:193] directed at exon 53 acceptor splice site. This antisense oligonucleotide was able to induce exon 53 skipping at 5, 100, 300 and 600 nM. A "cocktail" of three exon 53 antisense oligonucleotides: H53A(+23+47) [SEQ ID NO:195], H53A(+150+176) [SEQ ID NO:196] and H53D(+14-07) [SEQ ID NO:194], was also tested, as shown in Figure 20 and exhibited an ability to induce exon skipping.

Table 39 below includes other antisense molecules tested at a concentration range of 50, 100, 300 and 600 nM. These antisense molecules showed varying ability to induce exon 53 skipping. Antisense molecule H53A(+39+69) [SEQ ID NO:193] induced the strongest exon 53 skipping.

SEQ ID	Antisense oligonucleotide name	Sequence	Ability to induce skipping
191	H53A(+45+69)	CAU UCA ACU GUU GCC UCC GGU UCU G	Faint skipping at 50 nM
192	H53A(+39+62)	CUG UUG CCU CCG GUU CUG AAG GUG	Faint skipping at 50 nM
193	H53A(+39+69)	CAU UCA ACU GUU GCC UCC GGU UCU GAA GGU G	Strong skipping to 50 nM
194	H53D(+14-07)	UAC UAA CCU UGG UUU CUG UGA	Very faint skipping to 50 nM
195	H53A(+23+47)	CUG AAG GUG UUC UUG UAC UUC AUC C	Very faint skipping to 50 nM
196	H53A(+150+176)	UGU AUA GGG ACC CUC CUU CCA UGA CUC	Very faint skipping to 50 nM
197	H53D(+20-05)	CUA ACC UUG GUU UCU GUG AUU UUC U	Not made yet
198	H53D(+09-18)	GGU AUC UUU GAU ACU AAC CUU GGU UUC	Faint at 600 nM
199	H53A(-12+10)	AUU CUU UCA ACU AGA AUA AAA G	No skipping
200	H53A(-07+18)	GAU UCU GAA UUG UUU CAA CUA GAA U	No skipping
201	H53A(+07+26)	AUC CCA CUG AUU CUG AAU UC	No skipping
202	H53A(+124+145)	UUG GCU CUG GCC UGU CCU AAG A	No skipping

Table 39

**What is claimed is:**

1. An antisense molecule capable of binding to a selected target site to induce exon skipping in the dystrophin gene, as set forth in SEQ ID NO: 1 to 202.

## ABSTRACT

An antisense molecule capable of binding to a selected target site to induce  
5 exon skipping in the dystrophin gene, as set forth in SEQ ID NO: 1 to 214.

10



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Filing Date	Concurrently Herewith		
First Named Inventor	Stephen Donald WILTON		
Title	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		
Art Unit	N/A		
Examiner Name	Not Yet Assigned		
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Signature	/Amy E. Mandragouras, Esq./	Date (Optional)	September 14, 2017
Name	Amy E. Mandragouras, Esq.	Registration Number	36,207
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			
<b>NOTE:</b> This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.			
<input type="checkbox"/> *Total of <u>1</u> forms are submitted.			

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 14, 2017

Electronic Signature for Amy E. Mandragouras, Esq.: /Amy E. Mandragouras, Esq./

SRPT-VYDS-0003090

Doc Code: PA..

Document Description: Power of Attorney

PTO/AIA/82B (07-13)

Approved for use through 11/30/2014. OMB 0651-0051

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number

## POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☒ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above:

123147

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☒ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

Firm or Individual Name	Amy E. Mandragouras, Esq. NELSON MULLINS RILEY & SCARBOROUGH LLP				
Address	One Post Office Square				
City	Boston	State	MA	Zip	02109-2127
Country	US				
Telephone	(800) 237-2000	Email	ipboston.docketing@nelsonmullins.com		

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

The University of Western Australia

☐ Inventor or Joint Inventor (title not required below)

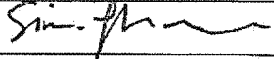
☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

### SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	16/May/14
Name	Simon J. Handford		
Title	Associate Director, Research Development and Innovation		

**NOTE:** Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of 1 forms are submitted.

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>				
<b>Filing Date:</b>				
<b>Title of Invention:</b>		ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF		
<b>First Named Inventor/Applicant Name:</b>		Stephen Donald WILTON		
<b>Filer:</b>		Amy E. Mandragouras		
<b>Attorney Docket Number:</b>		AVN-008CN41		
Filed as Small Entity				
<b>Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)</b>				
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**Electronic Acknowledgement Receipt**

<b>EFS ID:</b>	30370252
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<b>International Application Number:</b>	
<b>Confirmation Number:</b>	2879
<b>Title of Invention:</b>	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF
<b>First Named Inventor/Applicant Name:</b>	Stephen Donald WILTON
<b>Customer Number:</b>	123147
<b>Filer:</b>	Amy E. Mandragouras
<b>Filer Authorized By:</b>	
<b>Attorney Docket Number:</b>	AVN-008CN41
<b>Receipt Date:</b>	14-SEP-2017
<b>Filing Date:</b>	
<b>Time Stamp:</b>	20:18:17
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
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RAM confirmation Number	091517INTEFSW00006202120080
Deposit Account	120080
Authorized User	Amy Mandragouras

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.21 (Miscellaneous fees and charges)

**File Listing:**

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Case 1:21-cv-01015-JLH Document 434-3 Filed 12/18/23 Page 114 of 224 PageID #: 32608

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<p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					

DocCode – SCORE

## SCORE Placeholder Sheet for IFW Content

Application Number: 15705172

Document Date: 09/14/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Drawing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via eDAN using the Supplemental Content tab, or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: August 26, 2013

SRPT-VYDS-0003097

DocCode – SEQ.TXT

## SCORE Placeholder Sheet for IFW Content

Application Number: 15705172

Document Date: 09/14/2017

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

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- Sequence Listing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via eDAN using the Supplemental Content tab, or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

Form Revision Date: August 26, 2013

SRPT-VYDS-0003098

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 15, 2017  
Electronic Signature for Amy E. Mandragouras, Esq.: /Amy E. Mandragouras, Esq./

Docket No.: AVN-008CN41  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Stephen Donald Wilton *et al.*

Application No.: 15/705,172

Confirmation No.: 2879

Filed: September 14, 2017

Art Unit: 1674

For: ANTISENSE OLIGONUCLEOTIDES FOR  
INDUCING EXON SKIPPING AND  
METHODS OF USE THEREOF

Examiner: Not Yet Assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115**

Dear Sir:

Prior to examination on the merits, please amend the above-identified U.S. patent application as follows:

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Remarks/Arguments** begin on page 3 of this paper.

Application No.: 15/705,172

Docket No.: AVN-008CN41

**AMENDMENTS TO THE CLAIMS**

1. **(Canceled)**

2. **(New)** An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69), wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

3. **(New)** A pharmaceutical composition comprising: (i) an antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69), wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping, or a pharmaceutically acceptable salt thereof; and (ii) a pharmaceutically acceptable carrier.

Application No.: 15/705,172

Docket No.: AVN-008CN41

**REMARKS**

Claim 1 was pending in the application. Claim 1 has been cancelled without disclaimer or prejudice to further prosecution in this or a related application. New claims 2 and 3 have been added.

Support for the new claims can be found throughout the specification and claims as originally filed. Specifically, support for the term "morpholino antisense oligonucleotide" can be found at page 17, lines 1-5 (Table 1A) of the specification. Morpholino antisense oligonucleotides have been described in the literature. See, *e.g.*, Summerton, J. and Weller, D. (1997) Morpholino Antisense oligomers: design, preparation, and properties. *Antisense Nucl. Acid Drug Dev.*, 7, 187-195; Heasman, J. (2002) Morpholino Oligos: making sense of antisense? *Dev Biol* 243:209-214; and Gebiski, B. *et al.* (2003) Morpholino antisense oligonucleotide induced dystrophin exon 23 skipping in *mdx* mouse muscle. *Hum. Mol. Gen.* 12(15): 1801-1811.

No new matter has been added. Accordingly, following entry of the foregoing amendment claims 2 and 23 will be pending in the application.



Application No.: 15/705,172

Docket No.: AVN-008CN41

**CONCLUSION**

In view of the foregoing, Applicants respectfully submit that the pending claims are in condition for allowance. If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 217-4626. If a fee is due with this submission, please charge our Deposit Account No. 12-0080 under Order No. AVN-008CN41, from which the undersigned is authorized to draw.

Dated: September 15, 2017

Respectfully submitted,  
Electronic signature: /Amy E. Mandragouras,  
Esq./  
Amy E. Mandragouras, Esq.  
Registration No.: 36,207  
NELSON MULLINS RILEY & SCARBOROUGH LLP  
One Post Office Square  
Boston, Massachusetts 02109-2127  
(617) 217-4626  
(617) 217-4699 (Fax)  
Attorney/Agent For Applicant

**Electronic Acknowledgement Receipt**

<b>EFS ID:</b>	30375165
<b>Application Number:</b>	15705172
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	2879
<b>Title of Invention:</b>	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF
<b>First Named Inventor/Applicant Name:</b>	Stephen Donald WILTON
<b>Customer Number:</b>	123147
<b>Filer:</b>	Amy E. Mandragouras/Jackeline Flores
<b>Filer Authorized By:</b>	Amy E. Mandragouras
<b>Attorney Docket Number:</b>	AVN-008CN41
<b>Receipt Date:</b>	15-SEP-2017
<b>Filing Date:</b>	
<b>Time Stamp:</b>	14:04:58
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

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1	Preliminary Amendment	2017-09-15_Preliminary-Amendment_AVN-008CN41.pdf	33707 18ceb3fdc3f702988312603eb6da08e38056fb2b	no	4

**Warnings:**

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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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Sequence Listing was accepted.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Anjum, Durreshwar

Timestamp: [year=2017; month=9; day=20; hr=10; min=32; sec=59; ms=759; ]

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Application No: 15705172 Version No: 1.0

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<210> 18

<211> 24

<212> RNA

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<211> 20

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<210> 20

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<210> 22

<211> 30

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<210> 23

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<210> 26

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<210> 28

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<210> 30

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<210> 31

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<210> 32

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<210> 34

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<210> 55

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<212> RNA

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Human 2'-O-methyl phosphorothioate antisense  
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<210> 57

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<210> 58

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<210> 59

<211> 20

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<210> 60

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Doc code: IDS

# 32636

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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	1	2000-325085	JP	A	2000-11-28	MATSUO MASAFUMI, ET AL.		
	2	2002-010790	JP	A	2002-01-15	Matsuo Masafumi		×
	3	2002-325582	JP	A	2002-11-12	MATSUO, MASAFUMI, ET AL.		□

Application Number # 32637		15/05172
Filing Date		2017-09-14
First Named Inventor	Stephen Donald WILTON	
Art Unit	1674	
Examiner Name	Not Yet Assigned	
Attorney Docket Number	AVN-008CN41	

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

4	2002-340857	JP	A	2002-11-27	Matsushita Electric Ind Co Ltd	<input checked="" type="checkbox"/>
5	2002-529499	JP	A	2002-09-10	Eli Lilly and Company	<input checked="" type="checkbox"/>
6	2004-509622	JP	A	2004-04-02	Academisch Ziekenhuis Leiden	<input checked="" type="checkbox"/>
7	2010-268815	JP	A	2010-12-02	MATSUO MASAFUMI	<input type="checkbox"/>
8	2011-101655	JP	A	2011-05-26	Academisch Ziekenhuis Leiden	<input checked="" type="checkbox"/>
9	2011-200235	JP	A	2011-10-13	Academisch Ziekenhuis Leiden	<input checked="" type="checkbox"/>
10	2014-054250	JP	A	2014-03-27	Nippon Shinyaku Co Ltd,	<input checked="" type="checkbox"/>
11	2014-111638	JP	A	2014-06-19	Academisch, Ziekenhuis Leiden et al.	<input checked="" type="checkbox"/>
12	2014-138589	JP	A	2014-07-31	Academisch, Ziekenhuis Leiden	<input checked="" type="checkbox"/>
13	4777777	JP	B2	2011-09-21	Kobe University	<input checked="" type="checkbox"/>
14	4846965	JP	B2	2011-12-28	ACADEMISCH ZIEKENHUIS LEIDEN	<input type="checkbox"/>

Application Number  
# 32638

15/05172

Filing Date

2017-09-14

First Named Inventor

Stephen Donald WILTON

Art Unit

1674

Examiner Name

Not Yet Assigned

Attorney Docket Number

AVN-008CN41

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STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

15	5138722	JP	B2	2013-02-06	Matsuo Masafumi,	<input checked="" type="checkbox"/>
16	5378423	JP	B2	2013-12-25	ACADEMISCH ZIEKENHUIS LEIDEN	<input type="checkbox"/>
17	00/15780	WO	A1	2000-03-23	University College London	<input type="checkbox"/>
18	00/44897	WO	A1	2000-08-03	AVI Biopharma, Inc.	<input type="checkbox"/>
19	00/78341	WO	A1	2000-12-28	Murdoch Childrens Research Institute	<input type="checkbox"/>
20	01/49775	WO	A2	2001-07-12	AVI Biopharma, Inc.	<input type="checkbox"/>
21	01/72765	WO	A1	2001-10-04	ISIS Pharmaceuticals, Inc.	<input type="checkbox"/>
22	01/83503	WO	A2	2001-11-08	Hybridon, Inc	<input type="checkbox"/>
23	01/83740	WO	A2	2001-11-08	AVI Biopharma, Inc.	<input type="checkbox"/>
24	02/018656	WO	A2	2002-03-07	AVI Biopharma, Inc.	<input type="checkbox"/>
25	02/24906	WO	A1	2002-03-28	Academisch Ziekenhuis Leiden	<input type="checkbox"/>

Application Number # 32639		15/05172
Filing Date		2017-09-14
First Named Inventor	Stephen Donald WILTON	
Art Unit	1674	
Examiner Name	Not Yet Assigned	
Attorney Docket Number	AVN-008CN41	

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STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

26	02/29406	WO	A1	2002-04-11	Murto, James	<input type="checkbox"/>
27	03/053341	WO	A2	2003-07-03	Isis Pharmaceuticals, Inc.	<input type="checkbox"/>
28	04/048570	WO	A1	2004-06-10	Kobe University	<input checked="" type="checkbox"/>
29	04/083432	WO	A1	2004-09-30	Academisch Ziekenhuis Leiden	<input type="checkbox"/>
30	04/083446	WO	A2	2004-09-30	Academisch Ziekenhuis Leiden	<input type="checkbox"/>
31	2005/115479	WO	A2	2005-12-08	Avi Biopharma, Inc	<input type="checkbox"/>
32	2006/000057	WO	A1	2006-01-05	University of Western Australia	<input type="checkbox"/>
33	2006/021724	WO	A2	2006-03-02	Genethon et al.	<input checked="" type="checkbox"/>
34	2006/112705	WO	A2	2006-10-26	Academisch Ziekenhuis Leiden	<input type="checkbox"/>
35	2007/058894	WO	A2	2007-05-24	The University of North Carolina at Chapel Hill et	<input type="checkbox"/>
36	2007/133812	WO	A2	2007-11-22	Philadelphia Health & Education Corporation, D/ B/A	<input type="checkbox"/>



Application Number # 32640		15/05172
Filing Date		2017-09-14
First Named Inventor	Stephen Donald WILTON	
Art Unit	1674	
Examiner Name	Not Yet Assigned	
Attorney Docket Number	AVN-008CN41	

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STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

37	2007/135105	WO	A1	2007-11-29	Academisch Ziekenhuis Leiden	<input type="checkbox"/>
38	2008/036127	WO	A2	2008-03-27	Avi Biopharma, Inc.	<input type="checkbox"/>
39	2009/054725	WO	A2	2009-04-30	Academisch Ziekenhuis Leiden et al.	<input type="checkbox"/>
40	2009/101399	WO	A1	2009-08-20	Isis Innovation Limited	<input type="checkbox"/>
41	2009/139630	WO	A2	2009-11-19	Prosensa Technologies B.V. et al.	<input type="checkbox"/>
42	2010/048586	WO	A1	2010-04-29	AVI Biopharma, Inc.	<input type="checkbox"/>
43	2010/050801	WO	A1	2010-05-06	Prosensa Technologies B.V. et al.	<input type="checkbox"/>
44	2010/050802	WO	A2	2010-05-06	Academisch Ziekenhuis Leiden et al.	<input type="checkbox"/>
45	2010/115993	WO	A1	2010-10-14	Association Institut de Myologie et al.	<input type="checkbox"/>
46	2010/123369	WO	A1	2010-10-28	Prosensa Technologies B.V.	<input type="checkbox"/>
47	2010/136415	WO	A1	2010-12-02	Universita Degli Studi di Roma "La Sapienza"	<input type="checkbox"/>

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32641	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

48	2010/136417	WO	A1	2010-12-02	Universita Degli Studi di Roma "La Sapienza"	<input type="checkbox"/>
49	2010/150231	WO	A1	2010-12-29	Universita Degli Studi di Ferrara	<input type="checkbox"/>
50	2011/024077	WO	A2	2011-03-03	Inserm (Institut National de la Sante et de la Rec	<input type="checkbox"/>

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	1	AON PS1966 Mass Spectrometry Data, Pages 8, Exhibit Number 1154 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	2	AON PS1966 UPLC Data, Pages 2, Exhibit Number 1165 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	3	AON PS1967 Mass Spectrometry Data, Pages 7, Exhibit Number 1155 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	4	AON PS1967 UPLC Data, Pages 2, Exhibit Number 1166 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	5	AON PS229 (h53AON1) HPLC Chromatograph Pages 2, Exhibit Number 1140 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	6	AON PS229 (h53AON1) HPLC Method Report, Pages 3, Exhibit Number 1139 filed in Interferences 106,007 and 106,008 on February 16, 2015.	

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32642	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

7	AON PS229 (h53AON1) Mass Spectrometry Data, Pages 3, Exhibit Number 1142 filed in Interferences 106,007 and 106,008 on February 16, 2015.
8	AON PS229 (h53AON1) Synthesis Laboratory Notebook Entry, Pages 1, Exhibit Number 1137 filed in Interferences 106,007 and 106,008 on February 16, 2015.
9	AON PS229L (h53AON229L) Certificate of Analysis, Pages 1, Exhibit Number 1129 filed in Interferences 106,007 and 106,008 on February 17, 2015.
10	AON PS43 (h51AON1) Certificate of Analysis, Pages 1, Exhibit Number 1134 filed in Interferences 106,007 and 106,008 on February 16, 2015.
11	AON PS43 (h51AON1) HPLC Chromatogram, Pages 1, Exhibit Number 1131 filed in Interferences 106,007 and 106,008 on February 17, 2015.
12	AON PS43 (h51AON1) HPLC Method Report, Pages 4, Exhibit Number 1130 filed in Interferences 106,007 and 106,008 on February 17, 2015.
13	AON PS43 (h51AON1) Mass Spectrometry Data, Pages 3, Exhibit Number 1135 filed in Interferences 106,007 and 106,008 on February 16, 2015.
14	AON PS43 (h51AON1) UPLC-UV Data, Pages 2, Exhibit Number 1136 filed in Interferences 106,007 and 106,008 on February 16, 2015.
15	AONs PS1958, PS1959, PS1960, PS1961, PS1962, PS1963, PS1964, PS1965, PS1966, and PS1967 HPLC Method Report, Pages 3, Exhibit Number 1143 filed in Interferences 106,007 and 106,008 on February 16, 2015.
16	Applicant-Initiated Interview Summary dated April 8, 2013 in U.S. Application Serial No. 13/094,548, (University of Western Australia Exhibit 2144, filed April 3, 2015 in Interferences 106007, 106008, and 106013, pages 1-11).
17	Arechavala-Gomez V, et al., "Immunohistological intensity measurements as a tool to assess sarcolemma-associated protein expression," Neuropathol Appl Neurobiol 2010;36: 265-74.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32643	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

18	ARECHAVALA-GOMEZA, V. et al., "Comparative Analysis of Antisense Oligonucleotide Sequences for Targeted Skipping of Exon 51 During Dystrophin Pre-mRNA Splicing in Human Muscle," Human Gene Therapy, Vol. 18:798-810 (2007)
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32644	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
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Application Number # 32645	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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44	Claim Chart 13/550,210, Pages 45, Exhibit Number 1217 filed in Interferences 106,007 and 106,008 on February 17, 2015.
45	Claim Chart, US 7,807,816, 14 pages (Exhibit Number 1063 filed in interferences 106008, 106007 on November 18, 2014)
46	Claim Chart, US 7,960,541, 17 pages (Exhibit Number 1064 filed in interferences 106008, 106007 on November 18, 2014)
47	Claim Chart, US 8,455,636, 32 pages (Exhibit Number 1062 filed in interferences 106008, 106007 on November 18, 2014)
48	Claim Comparison Chart - Claims 11 and 29 in 13/550,210, Pages 1, Exhibit Number 1226 filed in Interferences 106,007 and 106,008 on February 17, 2015.
49	Claim Comparison Chart 13/550,210 vs 11/233,495, Pages 12, Exhibit Number 1218 filed in Interferences 106,007 and 106,008 on February 17, 2015.
50	Claim Comparison Chart 13/550,210 vs 12/198,007, Pages 1, Exhibit Number 1219 filed in Interferences 106,007 and 106,008 on February 17, 2015.

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Application Number # 32846	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
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Application Number # 32647	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

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	Filing Date		2017-09-14
	First Named Inventor		Stephen Donald WILTON
	Art Unit		1674
	Examiner Name		Not Yet Assigned
	Attorney Docket Number		AVN-008CN41

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	1	2011/045747	WO	A1	2011-04-21	Universita Delgi Studi Di Ferrara		
	2	2011/057350	WO	A1	2011-05-19	The University of Western Australia		
	3	2011/143008	WO	A1	2011-11-17	The Charlotte-Mecklenburg Hospital Authority D/B/A		

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Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

4	2012/001941	WO	A1	2012-01-05	Hagiwara, Masatoshi et al.	<input checked="" type="checkbox"/>
5	2012/029986	WO	A1	2012-03-08	Nippon Shinyaku Co., Ltd. et al.	<input type="checkbox"/>
6	2012/043730	WO	A1	2012-04-05	Nippon Shinyaku Co., Ltd.	<input checked="" type="checkbox"/>
7	2012/109296	WO	A1	2012-08-16	The Charlotte-Mecklenburg Hospital Authority D/B/A	<input type="checkbox"/>
8	2012/150960	WO	A1	2012-11-08	Avi Biopharma, Inc	<input type="checkbox"/>
9	2013/033407	WO	A2	2013-03-07	The Regents of the University of California	<input type="checkbox"/>
10	2013/053928	WO	A1	2013-04-18	Association Institut De Myologie et al.	<input type="checkbox"/>
11	2013/100190	WO	A1	2013-07-04	Nippon Shinyaku Co., Ltd. et al.	<input checked="" type="checkbox"/>
12	2013/112053	WO	A1	2013-08-01	Prosensa Technologies B.V.	<input type="checkbox"/>
13	2013/142087	WO	A1	2013-09-26	Sarepta Therapeutics, Inc	<input type="checkbox"/>
14	2014/007620	WO	A2	2014-01-09	Prosensa Technologies B.V.	<input type="checkbox"/>

Application Number  
# 32651

15/05172

Filing Date

2017-09-14

First Named Inventor

Stephen Donald WILTON

Art Unit

1674

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AVN-008CN41

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

15	2014/100714	WO	A1	2014-06-26	Sarepta Therapeutics, Inc	<input type="checkbox"/>
16	2014/144978	WO	A2	2014-09-18	Sarepta Therapeutics, Inc	<input type="checkbox"/>
17	2014/153220	WO	A2	2014-09-25	Sarepta Therapeutics, Inc	<input type="checkbox"/>
18	2014/153240	WO	A2	2014-09-25	Sarepta Therapeutics, Inc	<input type="checkbox"/>
19	2014/172669	WO	A1	2014-10-23	Res Inst At Nationwide Children S Hospital	<input type="checkbox"/>
20	2017/059131	WO	A1	2017-04-06	Sarepta Therapeutics, Inc	<input type="checkbox"/>
21	93/20227	WO	A1	1993-10-14	Abbott Laboratories	<input type="checkbox"/>
22	94/02595	WO	A1	1994-02-03	Ribozyme Pharmaceuticals, Inc.	<input type="checkbox"/>
23	94/26887	WO	A1	1994-11-24	The University of North Carolina at Chapel Hill	<input type="checkbox"/>
24	96/10391	WO	A1	1996-04-11	The University of British Columbia	<input type="checkbox"/>
25	96/10392	WO	A1	1996-04-11	The University of British Columbia	<input type="checkbox"/>

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32652	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
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Attorney Docket Number	AVN-008CN41

26	97/30067	WO	A1	1997-08-21	Isis Pharmaceuticals, Inc.	<input type="checkbox"/>
27	97/34638	WO	A1	1997-09-25	The Regents of the University of California	<input type="checkbox"/>

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**NON-PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>5</sup>
	1	Classification Excerpts from USPC System, 21 pages, (Academisch Ziekenhuis Leiden Exhibit 1234, filed May 5, 2015 in Interference 106007 and 106008).	
	2	COLLINS, C.A. et al., "Duchenne's muscular dystrophy: animal models used to investigate pathogenesis and develop therapeutic strategies," Int. J. Exp. Pathol., Vol. 84(4):165-172 (2003)	
	3	Confirmation of Dystrophin Exon 48 to 50 Deletion in Cell Line 8036 Laboratory Notebook Entry, Pages 3, Exhibit Number 1167 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	4	Confirmation of Dystrophin Exon 52 Deletion in Cell Line R1809 Laboratory; Notebook Entry, Pages 3, Exhibit Number 1168 filed in Interferences 106,007 and 106,008 on February 16, 2015.	
	5	Confirmatory Study of Eteplirsen in DMD Patients, An Open-Label, Multi-Center, 48-Week Study With a Concurrent Untreated Control Arm to Evaluate the Efficacy and Safety of Eteplirsen in Duchenne Muscular Dystrophy ,Clinical Trials.gov, Clinical Trial Identifier NCT02255552, October 1, 2014, 3 pages	
	6	Coolidge v. Efendic, 2008 WL 2080735, Int. No. 105,457 (BPAI May 16, 2008), 42 pages, (Academisch Ziekenhuis Leiden Exhibit 1235, filed May 5, 2015 in Interference 106007 and 106008).	
	7	COREY, David R. et al., "Morpholino antisense oligonucleotides: tools for investigating vertebrate development," Genome Biology, Vol. 2(5):1015.1 - 1015.3 (2001) (Exhibit Number 1026 filed in interferences 106008, 106007 on November 18, 2014)	

**INFORMATION DISCLOSURE  
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Art Unit	1674
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Attorney Docket Number	AVN-008CN41

8	Corrected Priority Statement filed by UWA in Int. No. 106,008 (as PN 219), Pages 5, Exhibit Number 1002 filed in Interference 106,013 on February 17, 2015.
9	Cortes et al., "Mutations in the conserved loop of human U5 snRNA generate use of novel cryptic 5' splice sites in vivo," EMBO J., Vol. 12, No. 13, pp. 5181-5189 (1993), Exhibit Number 1187 filed in Interferences 106,007 and 106,008 on February 17, 2015.
10	CROOKE, Stanley T., Antisense Drug Technology, Principles, Strategies, and Applications, Marcel Dekker, Inc., New York, Chapters 15 and 16, pages 375-389, 391-469 (2001) (Exhibit Number 2075 filed in interferences 106008, 106013, 106007 on November 18, 2014)
11	Curriculum Vitae of Judith van Deutekom, Pages 6, Exhibit Number 1126 filed in interferences 106,007 and 106,008 on February 17, 2015.
12	Curriculum Vitae, Erik Joseph Sontheimer, 18 pages, dated September 29, 2014 (Exhibit Number 1013 filed in interferences 106008, 106007 on November 18, 2014)
13	CV, Professor Matthew J.A. Wood, 3 pages (Exhibit Number 2003 filed in interferences 106008, 106007 on November 18, 2014)
14	DAVIS, Richard J. et al., "Fusion of PAX7 to FKHR by the Variant t(1;13)(p36;q14) Translocation in Alveolar Rhabdomyosarcoma," Cancer Research, Vol. 54:2869-2872 (1994) (Exhibit Number 1027 filed in interferences 106008, 106007 on November 18, 2014)
15	DE ANGELIS, Fernanda Gabriella et al., "Chimeric snRNA molecules carrying antisense sequences against the splice junctions of exon 51 of the dystrophic pre-mRNA induce exon skipping and restoration of a dystrophin synthesis in 48-50 DMD cells," PNAS, Vol. 99(14):9456-9461 (2002)
16	Decision on Appeal, Ex Parte Martin Gleave and Hideaki Miyake, Appeal No. 2005-2447, Appl. No. 09/619,908 (January 31, 2006) (2009 WL 6927761 (Bd.Pat.App.& Interf.), Pages 12, Exhibit Number 1207 filed in Interferences 106,007 and 106,008 on February 17, 2015.
17	Decision on Request for ReHearing, Ex Parte Roderick John Scott, Appeal No. 2008-004077, Appl. No. 10/058,825 (January 6, 2010) (2010 WL 191079 (Bd.Pat.App. & Interf.), Pages 21, Exhibit Number 1208 filed in Interferences 106,007 and 106,008 on February 17, 2015.
18	Declaration of Judith C.T. van Deutekom Under 37 C.F.R. §1.132, filed on January 27, 2012, in U.S. Patent Reexamination Control No 90/011,320, regarding U.S. Patent No. 7,534,879, (University of Western Australia Exhibit 2133, filed April 3, 2015 in Interferences 106007, 106008, and 106013, pages 1-10).



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Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

19	Declaration of Judith van Deutekom, Pages 45, Exhibit Number 1125 filed in interferences 106,007 and 106,008 on February 17, 2015.
20	DELLORUSSO, Christiana et al., "Functional correction of adult mdx mouse muscle using gutted adenoviral vectors expressing full-length dystrophin," PNAS, Vol. 99(20):12979-12984 (2002)
21	Deposition Transcript of Erik J. Sontheimer, Ph.D. of January 21, 2015 (99 pages), Exhibit Number 1215 filed in Interferences 106,007 and 106,008 on February 17, 2015.
22	Deposition Transcript of Matthew J. A. Wood, M.D., D. Phil., January 22, 2015, including Errata Sheet, Pages 198, Exhibit Number 1007 filed in Interference 106,013 on February 17, 2015.
23	Deposition Transcript of Matthew J. A. Wood, M.D., D. Phil., Pages 196, Exhibit Number 1122 filed in interferences 106,007 and 106,008 on February 17, 2015.
24	Desalting of Oligonucleotides, Pages 2, Exhibit Number 1132 filed in Interferences 106,007 and 106,008 on February 17, 2015.
25	DIRKSEN, Wessel P. et al., "Mapping the SF2/ASF Binding Sites in the Bovine Growth Hormone Exonic Splicing Enhancer," The Journal of Biological Chemistry, Vol. 275(37):29170-29177 (2000)
26	DOMINSKI, Zbigniew et al., "Identification and Characterization by Antisense Oligonucleotides of Exon and Intron Sequences Required for Splicing," Molecular and Cellular Biology, Vol. 14(11):7445-7454 (1994)
27	DOMINSKI, Zbigniew et al., "Restoration of correct splicing in thalassemic pre-mRNA by antisense oligonucleotides," Proc. Natl. Acad. Sci. USA, Vol. 90:8673-8677 (1993)
28	DORAN, Philip et al., "Proteomic profiling of antisense-induced exon skipping reveals reversal of pathobiochemical abnormalities in dystrophic mdx diaphragm," Proteomics, Vol. 9:671-685, DOI 10.1002/pmic.200800441 (2009)
29	DOUGLAS, Andrew G.L. et al., "Splicing therapy for neuromuscular disease," Molecular and Cellular Neuroscience, Vol. 56:169-185 (2013) (Exhibit Number 2005 filed in interferences 106008, 106013, 106007 on November 18, 2014)

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First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

30	Doyle, Donald F., et al. (2001) "Inhibition of Gene Expression Inside Cells by PeptideNucleic Acids: Effect of mRNA Target Sequence, Mismatched Bases, and PNA Length," Biochemistry 40:53-64, (Exhibit Number 2123 filed in Interferences 106,007 and 106,008 on February 17, 2015.
31	Dr. Wood Errata Sheet - 22 Jan 2015, Pages 2, Exhibit Number 1227 filed in Interferences 106,007 and 106,008 on February 17, 2015.
32	DUNCKLEY, Matthew G. et al., "Modification of splicing in the dystrophin gene in cultured Mdx muscle cells by antisense oligoribonucleotides," Human Molecular Genetics, Vol. 5(1):1083-1090 (1995)
33	DUNCKLEY, Matthew G. et al., "Modulation of Splicing in the DMD Gene by Antisense Oligoribonucleotides," Nucleosides & Nucleotides, Vol. 16(7-9):1665-1668 (1997)
34	ECKSTEIN, F., "Nucleoside Phosphorothioates," Ann. Rev. Biochem., Vol. 54:367-402 (1985) (Exhibit Number 1028 filed in interferences 106008, 106007 on November 18, 2014)
35	ELAYADI, Anissa N. et al., "Application of PNA and LNA oligomers to chemotherapy," Current Opinion in Investigational Drugs, Vol. 2(4):558-561 (2001)
36	Email from Danny Huntington to Interference Trial Section, dated September 21, 2014, Pages 2, Exhibit Number 3001 filed in Interference 106,007, 106,008, and 106,013 on September 26, 2014.
37	Email From Sharon Crane to Interference Trial Section, dated November 13, 2014, Pages 2, Exhibit Number 3002 filed in Interference 106,007, 106,008, and 106,013 on dated November 14, 2014.
38	Emery, A.E. H., "Population frequencies of inherited neuromuscular diseases - a world survey," Neuromuscul Disord 1991;1:19-29.
39	Errata sheet for the January 22, 2015 deposition of Matthew J. A. Wood, M.D., D. PHIL., 2 pages, (Exhibit Number 2128 filed in interferences 106,007 and 106,008 on February 17, 2015.
40	Errata sheet for the March 12, 2015 deposition of Erik J. Sontheimer, Ph.D., (University of Western Australia Exhibit 2149, filed April 3, 2015 in Interferences 106007, 106008, and 106013, page 1).

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32656	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

41	Errata to the Sarepta Briefing Information for the April 25, 2016 Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee, Eleplirsen Errata Document, NDA 206488, 5 pages.
42	ERRINGTON, Stephen J. et al., "Target selection for antisense oligonucleotide induced exon skipping in the dystrophin gene," The Journal of Gene Medicine, Vol. 5:518-527 (2003)
43	European Office Action for Application No. 09752572.9, 5 pages, dated February 29, 2012
44	European Response, Application No. 10004274.6, 7 pages, dated November 5, 2013 (Exhibit Number 1060 filed in Interferences 106008, 106007 on November 18, 2014)
45	European Response, Application No. 12198517.0, 7 pages, dated October 21, 2014 (Exhibit Number 2084 filed in Interferences 106008, 106013, 106007 on November 18, 2014)
46	European Search Report for Application No. 10004274.6, 12 pages, dated January 2, 2013
47	European Search Report, EP15168694.6, dated July 23, 2015, pages 1-8.
48	Excerpts from Prosecution History of Application No. 13/741,150: Notice of Allowance dated March 16, 2015; List of References cited by Applicant and Considered by Examiner; Notice of Allowance and Fees due dated September 18, 2014; Amendment in Response to Non-Final Office Action dated July 11, 2014, (Academisch Ziekenhuis Leiden Exhibit 1229, filed April 3, 2015 in Interference 106007 and 106008, pages 1-133).
49	Excerpts from Prosecution History of Application No. 13/826,880: Notice of Allowance dated January 26, 2015 and Amendment in Response to Non-Final Office Action dated October 15, 2014, (Academisch Ziekenhuis Leiden Exhibit 1228, filed April 3, 2015 in Interference 106007 and 106008, pages 1-16).
50	Excerpts from Yeo (Ed.), "Systems Biology of RNA Binding Proteins," Adv. Exp. Med. Biol., Chapter 9, 56 pages (2014), (Academisch Ziekenhuis Leiden Exhibit 1232, filed April 3, 2015 in Interference 106007 and 106008, pages 1-56).

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**INFORMATION DISCLOSURE  
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( Not for submission under 37 CFR 1.99)

Application Number # 32657	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

**EXAMINER SIGNATURE**

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STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32658	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

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☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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# 32660

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32861	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	Excerpts of SEC Form 8-K, dated November 23 2014, for BioMarin Pharmaceutical Inc., (University of Western Australia Exhibit 2129, filed April 3, 2015 in Interferences 106007, 106008, and 106013, pages 1-9).
2	Exon 46 Sequence of Dystrophin, Document D18 as filed in Opposition of European Patent EP1619249, filed June 23, 2009, 1 page
3	Exon 51 Internal Sequence Schematic, Pages 1, Exhibit Number 1224 filed in Interferences 106,007 and 106,008 on February 17, 2015.
4	Exon 53 Internal Sequence Schematic, Pages 1, Exhibit Number 1225 filed in Interferences 106,007 and 106,008 on February 17, 2015.
5	Extended European Search Report, EP 15190341.6, dated April 28, 2016, 9 pages.
6	Fairclough et al., "Therapy for Duchenne muscular dystrophy: renewed optimism from genetic approaches," Nature Reviews, Vol. 14, pp. 373-378 (June, 2013), Exhibit Number 1112 filed in interferences 106,007 and 106,008 on February 17, 2015.
7	FALL, Abbie M. et al., "Induction of revertant fibres in the mdx mouse using antisense oligonucleotides," Genetics Vaccines and Therapy, Vol. 4:3, doi:10.1186/1479-0556-4-3, 12 pages (2006)
8	FDA Briefing Document, "Peripheral and Central Nervous System," Drugs Advisory Committee Meeting, NDA 206488 Eteplirsen, Food and Drug Administration, pages 1-73, January 22, 2016.
9	FDA Briefing Information for the April 25, 2016 Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee, Eteplirsen, NDA 206488, 115 pages
10	FDA News Release, "FDA grants accelerated approval to first drug for Duchenne muscular dystrophy," September 19, 2016, 3 pages.
11	Federal Register, Vol. 58, No. 183, pp. 49432-49434, September 23, 1993 (6 pages); [Cited as: 58 FR 49432-01, 1993 WL 371451 (F.R.)], Exhibit Number 1221 filed in Interferences 106,007 and 106,008 on February 17, 2015.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32862	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	Federal Register, Vol. 69, No. 155, pp. 49960-50020 dated August 12, 2004 (62 pages), Exhibit Number 1220 filed in Interferences 106,007 and 106,008 on February 17, 2015.
13	FEENER, C. et al., "Alternative splicing of human dystrophin mRNA generates isoforms at the carboxy terminus," Nature, vol. 338:509 - 511 (1989).
14	File Excerpt from AZL U.S. Patent Application 11/233,495: Amendment After Non-Final Office Action, as-filed November 1, 2010 (Exhibit Number 1085 filed in interferences 106008, 106007 on December 23, 2014)
15	File Excerpt from AZL U.S. Patent Application 11/233,495: Claims examined in Non-Final Office Action, dated December 1, 2008 (Exhibit Number 1079 filed in interferences 106008, 106007 on December 23, 2014)
16	File Excerpt from AZL U.S. Patent Application 11/233,495: Final Office Action dated August 31, 2010 (Exhibit Number 1086 filed in interferences 106008, 106007 on December 23, 2014)
17	File Excerpt from U.S. Patent Application 11/233,495: Non-Final Office Action dated December 1, 2008 and Final Office Action dated June 25, 2009 (Exhibit Number 1078 filed in interferences 106008, 106007 on December 23, 2014)
18	File Excerpt from U.S. Patent Application No. 12/198,007: AZL's Preliminary Amendment and Response, as-filed November 7, 2008 (Exhibit Number 1075 filed in interferences 106008, 106007 on December 23, 2014)
19	File Excerpt from U.S. Patent Application No. 12/976,381: AZL's First Preliminary Amendment, as-filed December 22, 2010 (Exhibit Number 1076 filed in interferences 106008, 106007 on December 23, 2014)
20	File Excerpts from Prosecution History of U.S. Patent Application No. 13/270,992 ("UWA's U.S. Patent 8,486,907"), Pages 122, Exhibit Number 1006 filed in Interference 106,013 on February 17, 2015.
21	File Excerpts from U.S. Patent Application No. 11/233,495: Response to Non-Final Office Action, as filed July 26, 2011 (14 pages), Exhibit Number 1222 filed in Interferences 106,007 and 106,008 on February 17, 2015.
22	File Excerpts from U.S. Patent Application No. 13/270,992 ("UWA's U.S. Patent 8,486,907"): NFOA, dated 7/30/2012; Applicant-Initiated Interview Summary, dated 11/8/2012; Amendment, as filed January 30, 2013; NOA, dated 4/4/2013, Exhibit Number 1118 (122 pages) filed in interferences 106,007 and 106,008 on February 17, 2015.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32863	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

23	Flanagan, W. Michael, et al., "A cytosine analog that confers enhanced potency to antisense oligonucleotides," Proc. Nat'l Acad. Sci. USA, Vol. 96, pp. 3513-3518 (March, 1999), Exhibit Number 1211 filed in Interferences 106,007 and 106,008 on February 17, 2015.
24	Flanigan et al. (2003) "Rapid Direct Sequence Analysis of the Dystrophin Gene," Am. J. Hum. Genet. 72:931-939, dated February 17, 2015 (Exhibit Number 2120 filed in interferences 106,007 and 106,008 on February 17, 2015.
25	FLANIGAN, Kevin M. et al., "Pharmacokinetics and safety of single doses of drisapersen in non-ambulant subjects with Duchenne muscular dystrophy: Results of a double-blind randomized clinical trial," Neuromuscular Disorders, Vol. 24:16-24 (2014) (Exhibit Number 2038 filed in interferences 106008, 106013, 106007 on November 18, 2014)
26	Fletcher S., et al, "Morpholino oligomer-mediated exon skipping averts the onset of dystrophic pathology in the mdx mouse. Mol Ther 2007;15:1587-1592.
27	FLETCHER, Sue et al., "Dystrophin Isoform Induction In Vivo by Antisense-mediated Alternative Splicing," Molecular Therapy, Vol. 18(6):1218-1223 (2010)
28	FLETCHER, Sue et al., "Targeted Exon Skipping to Address 'Leaky' Mutations in the Dystrophin Gene," Molecular Therapy-Nucleic Acids, Vol. 1, e48, doi:10.1038/mtna.2012.40, 11 pages (2012)
29	FLETCHER, Susan et al., "Dystrophin expression in the mdx mouse after localised and systemic administration of a morpholino antisense oligonucleotide," J. Gene Med., Vol. 8:207-216 (2006)
30	FLETCHER, Susan et al., "Gene therapy and molecular approaches to the treatment of hereditary muscular disorders," Curr. Opin. Neurol., Vol. 13:553-560 (2000)
31	FOSTER, Helen et al., "Genetic Therapeutic Approaches for Duchenne Muscular Dystrophy," Human Gene Therapy, Vol. 23:676-687 (2012)
32	Fourth Declaration of Erik Sontheimer, Ph.D. (Pursuant to Bd.R. 41.155(b)(2) and SO 155.1.3 and 155.1.4), dated March 9, 2015, (University of Western Australia Exhibit 2138, filed April 3, 2015 in Interferences 106007, 106008, and 106013, pages 1-4).
33	FRAGALL, Clayton T. et al., "Mismatched single stranded antisense oligonucleotides can induce efficient dystrophin splice switching," BMC Medical Genetics, Vol. 12:141, 8 pages (2011) (Exhibit Number 2019 filed in interferences 106008, 106013, 106007 on November 18, 2014)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32884	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	FRALEY, Robert et al., "New generation of liposomes: the engineering of an efficient vehicle for intracellular delivery of nucleic acids," Trends Biochem., Vol. 6:77-80 (1981)
35	FRAZIER, Kendall S. et al., "Species-specific Inflammatory Responses as a Primary Component for the Development of Glomerular Lesions in Mice and Monkeys Following Chronic Administration of a Second-generation Antisense Oligonucleotide," Toxicologica Pathology, 13 pages (2013)
36	FRIEDMANN, Theodore, "Progress Toward Human Gene Therapy," Science, Vol. 244(4910):1275-1281 (1989)
37	GEBSKI, Bianca L. et al., "Morpholino antisense oligonucleotide induced dystrophin exon 23 skipping in mdx mouse muscle," Human Molecular Genetics, Vol. 12(15):1801-1811 (2003)
38	GenBank AF213437.1 Dated January 17, 2002
39	Generic Method for Average Mass Determination Using LC-UV-MS in the Negative Mode, Pages 15, Exhibit Number 1145 filed in Interferences 106,007 and 106,008 on February 16, 2015.
40	Generic UPLC Purity Method for Oligonucleotides (19- to 25-mers), Pages 18, Exhibit Number 1156 filed in Interferences 106,007 and 106,008 on February 16, 2015.
41	GENNARO, Alfonso R., (ed.), Remington's Pharmaceutical Sciences, 18th Edition, Mack Publishing, Co., Easton PA, 2020 pages (1990)
42	GILES, Richard V. et al., "Antisense Morpholino Oligonucleotide Analog Induces Missplicing of C-myc mRNA," Antisense & Nucleic Acid Drug Development, Vol. 9:213-220 (1999)
43	GlaxoSmithKline Press Release, Issued in London, UK, dated June 27, 2013 (5 pages), Exhibit Number 1202 filed in Interferences 106,007 and 106,008 on February 17, 2015.
44	GlaxoSmithKline, "GSK and Prosensa announce start of Phase III study of investigational Duchenne Muscular Dystrophy medication," press release, 6 pages, dated January 19, 2011 (Exhibit Number 2060 filed in interferences 106008, 106013, 106007 on November 18, 2014)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32665	15705172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

45	GlaxoSmithKline, "Prosensa regains rights to drisapersen from GSK and retains rights to all other programmes for the treatment of Duchenne muscular dystrophy (DMD), press release, 4 pages, dated January 13, 2014 (Exhibit 2040 in Interferences 106007, 106008, and 106013 on November 18, 2014).
46	GOEMANS, Nathalie M. et al., "Systemic Administration of PRO051 in Duchenne's Muscular Dystrophy," The New England Journal of Medicine, Vol. 364:1513-1522 (2011) (Exhibit Number 2036 filed in interferences 106008, 106013, 106007 on November 18, 2014)
47	Gordon et al., "Kinetic Characterization of the Second Step of Group II Intron Splicing: Role of Metal Ions and the Cleavage Site 2'-OH in Catalysis," Biochemistry, Vol. 39, pp. 12939-12952 (2000), Exhibit Number 1188 filed in Interferences 106,007 and 106,008 on February 17, 2015.
48	GORDON, Peter M. et al., "Metal ion catalysis during the exon-ligation step of nuclear pre-mRNA splicing: Extending the parallels between the spliceosome and group II introns," RNA, Vol. 6:199-205 (2000) (Exhibit Number 1055 filed in interferences 106008, 106007 on November 18, 2014)
49	GOYENVALLE, Aurelie et al., "Prevention of Dystrophic Pathology in Severely Affected Dystrophin/Utrophin-deficient Mice by Morpholino-oligomer-mediated Exon-skipping," Molecular Therapy, Vol. 18(1):198-205 (2010)
50	HAMMOND, Suzan M. et al., "Correlating In Vitro Splice Switching Activity With Systemic In Vivo Delivery Using Novel ZEN-modified Oligonucleotides," Molecular Therapy - Nucleic Acids, Vol. 3:1, 11 pages (2014) (Exhibit Number 2011 filed in interferences 106008, 106013, 106007 on November 18, 2014)

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STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32886	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

**CERTIFICATION STATEMENT**

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See attached certification statement.

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A certification statement is not submitted herewith.

**SIGNATURE**

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Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

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# 32668

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32869	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	Hammond, Suzan M., et al., "Genetic therapies for RNA mis-splicing diseases," Cell, Vol.27, No. 5, pp. 196-205 (May, 2011), Exhibit Number 1113 filed in interferences 106,007 and 106,008 on February 17, 2015.
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3	HARDING, PL et al., "The Influence of Antisense Oligonucleotide Length on Dystrophin Exon Skipping," Molecular Therapy, Vol. 15(1):157-166 (2007) (Exhibit Number 1030 filed in interferences 106008, 106007 on November 18, 2014)
4	Havenga et al., "Exploiting the Natural Diversity in Adenovirus Tropism for Therapy and Prevention of Disease," J. Virol., Vol. 76, No. 9, pp. 4612-4620 (May, 2002), Exhibit Number 1123 filed in interferences 106,007 and 106,008 on February 13, 2015.
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7	HEID, Christian A. et al., "Real Time Quantitative PCR," Genome Research, Vol. 6:986-994 (1996) (Exhibit Number 1061 filed in interferences 106008, 106007 on November 18, 2014)
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32870	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	HUSSEY, Nicole D. et al., "Analysis of five Duchenne muscular dystrophy exons and gender determination using conventional duplex polymerase chain reaction on single cells," Molecular Human Reproduction, Vol. 5(11):1089-1094 (1999)
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18	International Preliminary Report on Patentability, PCT/US2014/029610, dated July 1, 2015, pages 1-122.
19	International Preliminary Report on Patentability, PCT/US2014/029689, dated September 15, 2015, pages 1-10.
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21	International Search Report and Written Opinion of the International Searching Authority issued in International Patent Application No. PCT/US2013/077216 dated March 27, 2014
22	International Search Report and Written Opinion of the International Searching Authority issued in International Patent Application No. PCT/US2014/029610 dated September 18, 2014

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32671	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

23	International Search Report and Written Opinion of the International Searching Authority issued in International Patent Application No. PCT/US2014/029689, 8 pages, dated October 21, 2014
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26	International Search Report for Application No. PCT/AU2005/000943, 5 pages, dated October 20, 2005
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32672	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	JEARAWIRIYAPASARN, Natee et al., "Long-term improvement in mdx cardiomyopathy after therapy with peptide-conjugated morpholino oligomers," Cardiovascular Research, Vol. 85:444-453 (2010)
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36	Jett Foundation Presentation by McSherry, C. "Patient and Caregiver-Reported Outcomes of Patients in Clinical Trials of Eteplirsen for Treatment of Duchenne" at Peripheral and Central Nervous System Drugs Advisory Committee, April 25, 2016, 17 pages.
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40	KARRAS, James G. et al., "Deletion of Individual Exons and Induction of Soluble Murine Interleukin-5 Receptor-alpha Chain Expression through Antisense Oligonucleotide-Mediated Redirection of Pre-mRNA splicing," Molecular Pharmacology, Vol. 58:380-387 (2000)
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42	KINALI, Maria et al., "Local restoration of dystrophin expression with the morpholino oligomer AVI-4658 in Duchenne muscular dystrophy: a single-blind, placebo-controlled, dose-escalation, proof-of-concept study," Lancet Neurol., Vol. 8:918-928 (2009)
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32673	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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50	Lab-on-a-Chip Data, Pages 28, Exhibit Number 1185 filed in Interferences 106,007 and 106,008 on February 16, 2015.

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( Not for submission under 37 CFR 1.99)

Application Number # 32674	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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See attached certification statement.

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Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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# 32676

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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STATEMENT BY APPLICANT**  
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Application Number # 32877	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden Responsive Motion 4 (To Add Two New Claims), 65 pages, Patent Interference No. 106,007, (Doc 241), dated December 23, 2014.
2	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden Statement Regarding Oral Argument, filed in Patent Interference No. 106,013, April 10, 2015, pages 1-3 (Doc 189).
3	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden's Opposition 4 (To Not Exclude Evidence), filed in Patent Interference No. 106,007, May 5, 2015, pages 1-22 (Doc 465).
4	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden's Opposition 4 (To Not Exclude Evidence), filed in Patent Interference No. 106,008, May 5, 2015, pages 1-21 (Doc 473).
5	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden's Second Supplemental Notice of Real Party in Interest, filed in Patent Interference No. 106,007, May 28, 2015, pages 1-3, (Doc 468)
6	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden's Second Supplemental Notice of Real Party in Interest, filed in Patent Interference No. 106,008, May 28, 2015, pages 1-3, (Doc 476)
7	University of Western Australia v. Academisch Ziekenhuis Leiden, Academisch Ziekenhuis Leiden's Second Supplemental Notice of Real Party in Interest, filed in Patent Interference No. 106013, May 28, 2015, pages 1-3, (Doc 491)
8	University of Western Australia v. Academisch Ziekenhuis Leiden, ACADEMISH ZIEKENHUIS LEIDEN SUPPLEMENTAL NOTICE OF REAL PARTY IN INTEREST, Pages 3, DOC 149, Patent Interference No. 106,013 dated February 23, 2015.
9	University of Western Australia v. Academisch Ziekenhuis Leiden, ACADEMISH ZIEKENHUIS LEIDEN SUPPLEMENTAL NOTICE OF REAL PARTY IN INTEREST, Pages 3, Doc 413, Patent Interference No. 106,0007 dated February 23, 2015.
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32678	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Annotated Copy of Claims, Patent Interference No. 106,007, 15 pages, dated August 15, 2014 (Doc 15)
13	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Annotated Copy of Claims, Patent Interference No. 106,008, 14 pages, dated August 21, 2014 (Doc 14)
14	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Annotated Copy of Claims, Patent Interference No. 106,013, 14 pages, dated October 27, 2014 (Doc 16)
15	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Clean Copy of Claims and Sequence, filed in Patent Interference No. 106,013, 5 pages, dated October 15, 2014 (Doc 12)
16	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Corrected Notice of Related Proceedings, Patent Interference No. 106,007, 3 pages, dated August 1, 2014 (Doc 13)
17	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Exhibit List, 10 pages, Patent Interference No. 106,007 dated December 23, 2014 (Doc 240)
18	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL List of Exhibits, 9 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 209)
19	University of Western Australia v. Academisch Ziekenhuis Leiden, Azl List of Exhibits, as of November 18, 2014, 9 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 212)
20	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL List of Proposed Motions, Patent Interference No. 106,007, 6 pages, dated September 10, 2014 (Doc 16)
21	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL List of Proposed Motions, Patent Interference No. 106,008, 8 pages, dated September 10, 2014 (Doc 15)
22	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Motion 1 (For Judgment that UWA's Claims are Unpatentable Under 35 U.S.C. sections 102 and 103), 69 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 181)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32679	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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24	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Motion 2 (To Deny UWA the Benefit of AU 2004903474), 23 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 26)
25	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Motion 2 (To Deny UWA the Benefit of AU 2004903474), 24 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 29)
26	University of Western Australia v. Academisch Ziekenhuis Leiden, AZL Motion 3 (For Judgment of Unpatentability based on Myriad) 20 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 30)
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32680	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	University of Western Australia v. Academisch Ziekenhuis Leiden, Decision - Motions - 37 CFR § 41.125(a), filed in Patent Interference No. 106007, April 29, 2016, pages 1-53 (Doc 472)
35	University of Western Australia v. Academisch Ziekenhuis Leiden, Decision- Motions- 37 CFR§ 41.125(a), filed in Patent Interference No. 106,013, June 22, 2015, pages 1-12 (Doc 192).
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37	University of Western Australia v. Academisch Ziekenhuis Leiden, Decision-Rehearing -37 CFR § 41.125(c), filed in Patent Interference No. 106,013, December 29, 2015, pages 1-12 (Doc 202).
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40	University of Western Australia v. Academisch Ziekenhuis Leiden, Declaration of Interference, Patent Interference No. 106,008, 7 pages, dated July 24, 2014 (Doc 1)
41	University of Western Australia v. Academisch Ziekenhuis Leiden, Declaration of Interference, Patent Interference No. 106,013, 8 pages, dated September 29, 2014 (Doc 1)
42	University of Western Australia v. Academisch Ziekenhuis Leiden, Declaration of Matthew J.A. Wood, Patent Interference Nos. 106,007, 106,008 and 106,013, 184 pages, dated November 18, 2014 (Exhibit Number 2081 filed in Interferences 106008, 106013, 106007 on November 18, 2014)
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32681	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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48	University of Western Australia v. Academisch Ziekenhuis Leiden, Joint Stipulation Regarding Time Periods 4-6, 4 pages, Patent Interference No. 106013, (Doc 151), dated March 19, 2015.
49	University of Western Australia v. Academisch Ziekenhuis Leiden, Joint Stipulation Regarding Time Periods 4-6, 4 pages, Patent Interference No.106,008, (Doc 424 ), dated March 19, 2015.
50	University of Western Australia v. Academisch Ziekenhuis Leiden, Judgment-37 CFR § 41.127, 2 pages, Patent Interference No. 106,013, (Doc 197), dated September 29, 2015.

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**EXAMINER SIGNATURE**

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32682	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

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☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32685	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	University of Western Australia v. Academisch Ziekenhuis Leiden, Miscellaneous Order under 37 CFR 41.104(a), 4 pages, Patent Interference Nos. 106,007 and 106,008, dated December 15, 2014
2	University of Western Australia v. Academisch Ziekenhuis Leiden, Order - Authorizing Motions, Patent Interference No. 106,007, 3 pages, dated September 26, 2014 (Doc 20)
3	University of Western Australia v. Academisch Ziekenhuis Leiden, Order - Authorizing Motions, Patent Interference No. 106,007, 6 pages, dated September 23, 2014 (Doc 19)
4	University of Western Australia v. Academisch Ziekenhuis Leiden, Order - Authorizing Motions, Patent Interference No. 106,008, 6 pages, dated September 23, 2014 (Doc 18)
5	University of Western Australia v. Academisch Ziekenhuis Leiden, Order - Miscellaneous, 2 pages, Patent Interference Nos. 106,007, 106,008, 106,013, dated November 14, 2014
6	University of Western Australia v. Academisch Ziekenhuis Leiden, Order to Show Cause- 37 CFR§ 41.104(a), filed in Patent Interference No. 106,013, June 22, 2015, pages 1-3 (Doc 193).
7	University of Western Australia v. Academisch Ziekenhuis Leiden, Redecoration, Patent Interference No. 106,008, 2 pages, dated September 23, 2014 (Doc 19)
8	University of Western Australia v. Academisch Ziekenhuis Leiden, Second Declaration of Matthew J. A. Wood, M.D., D. PHIL., Patent Interference Nos. 106,007 and 106,008, 78 pages, dated February 17, 2015 (Exhibit Number 2116 filed in interferences 106,007 and 106,008, on February 17, 2015.
9	University of Western Australia v. Academisch Ziekenhuis Leiden, Statement Concerning Initial Settlement Discussions, 3 pages, Patent Interference No. 106,013, (Doc 136), dated December 30, 2014.
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32686	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	University of Western Australia v. Academisch Ziekenhuis Leiden, Statement Concerning Subsequent Settlement Discussions, filed in Patent Interference No. 106,013, August 24, 2015, pages 1-3 (Doc 195).
13	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Response to Order to Show Cause, filed in Patent Interference No. 106,013, July 20, 2015, pages 1-28 (Doc 194).
14	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Exhibit List as of April 10, 2015, filed in Patent Interference No. 106,007, April 10, 2015, pages 1-10 (Doc 456).
15	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Exhibit List as of April 10, 2015, filed in Patent Interference No. 106,008, April 10, 2015, pages 1-10 (Doc 464).
16	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Exhibit List as of April 3, 2015, filed in Interference 106007, April 3, 2015, pages 1-10 (Doc 431).
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18	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Exhibit List as of April 3, 2015, filed in Interference 106013, April 3, 2015, pages 1-10 (Doc 153).
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20	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Miscellaneous Motion 4 (to exclude evidence), filed in Patent Interference No. 106,007, April 10, 2015, pages 1-21 (Doc 455).
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32687	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

23	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Opposition 1 (Regarding Patentability Under 35 U.S.C. § 102/103), 39 pages, Patent Interference No. 106,008, (Doc 402), dated February 17, 2015
24	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Opposition 2 (To Retain UWA's Benefit of AU 2004903474), 31 pages, Patent Interference No. 106,008, (Doc 403), dated February 17, 2015
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28	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Opposition 4 (To deny entry of AZL's Proposed New Claims 104 and 105), 36 pages, Patent Interference No. 106,007, (Doc 397), dated February 17, 2015
29	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Opposition 4 (To deny entry of AZL's Proposed New Claims 30 and 31), 36 pages, Patent Interference No. 106,008, (Doc 405), dated February 17, 2015
30	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 1 (to AZL Opposition 1), filed April 3, 2015 in Interference 106007, pages 1-28 (Doc 428).
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
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Application Number # 32688	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 2 (to AZL Opposition 2) filed April 3, 2015 in Interference 106008, pages 1-22 (Doc 437).
35	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 3 (for Judgment under 35 U.S.C. §135(b)) filed April 3, 2015 in Interference 106008, pages 1-19 (Doc 438).
36	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 3 (to Institute an Interference) filed April 3, 2015 in Interference 106007, pages 1-17 (Doc 430).
37	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 4 (To Exclude Evidence), filed in Patent Interference No. 106,007, May 12, 2015, pages 1-13 (Doc 467).
38	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Reply 4 (To Exclude Evidence), filed in Patent Interference No. 106,008, May 12, 2015, pages 1-13 (Doc 475).
39	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Request for Oral Argument, filed in Patent Interference No. 106,007, April 10, 2015, pages 1-4 (Doc 457).
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41	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Request for Oral Argument, filed in Patent Interference No. 106,013, April 10, 2015, pages 1-3 (Doc 190).
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43	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Revised Designation of Lead and Backup Counsel, 4 pages, Patent Interference No. 106,007, (Doc 415), dated March 10, 2015.
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32689	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

45	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia Revised Designation of Lead and Backup Counsel, 5 pages, Patent Interference No. 106,008, (Doc 423 ), dated March 10, 2015.
46	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia, Exhibit List as of February 17, 2015, 8 pages, Patent Interference No. 106,007, (Doc No. 398) dated February 17, 2015.
47	University of Western Australia v. Academisch Ziekenhuis Leiden, University of Western Australia, Exhibit List as of February 17, 2015, 8 pages, Patent Interference No. 106,008, (Doc No. 406) dated February 17, 2015.
48	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Clean Copy of Involved Claims and Sequence, Patent Interference No. 106,007, 8 pages, dated August 1, 2014 (Doc 12)
49	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Clean Copy of Involved Claims and Sequence, Patent Interference No. 106,013, 7 pages, dated October 14, 2014 (Doc 7)
50	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Clean Copy of Involved Claims and Sequences, Patent Interference No. 106,008, 8 pages, dated August 7, 2014 (Doc 12)

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Examiner Signature		Date Considered	
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<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32690	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Doc code: IDS

# 32692

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32693	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Exhibit List as of November 18, 2014, 7 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 216)
2	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Exhibit list, 7 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 213)
3	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Exhibit list, 7 pages, Patent Interference No. 106,013, dated November 18, 2014 (Doc 134)
4	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Exhibit List, 7 pages, Patent Interference Nos. 106,008, dated December 12, 2014 (Doc 221)
5	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Exhibit List, 8 pages, Patent Interference No. 106,007, dated December 12, 2014 (Doc 217)
6	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA List of Proposed Motions, Patent Interference No. 106,007, 7 pages, dated September 10, 2014 (Doc 17)
7	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA List of Proposed Motions, Patent Interference No. 106,008, 6 pages, dated September 10, 2014 (Doc 16)
8	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Miscellaneous Motion 1 (for authorization to file terminal disclaimer), 5 pages, Patent Interference No. 106,008, dated October 17, 2014 (Doc 22)
9	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 1 (For Judgment Under 35 U.S.C., section 112(a)), 40 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 210)
10	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 1 (For Judgment Under 35 § 112(a)) Patent Interference No. 106,008 (Doc 213), 38 Pages, on November 18, 2014
11	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 1 (To Maintain Interference between UWA US Patent No. 8,486,907 and AZL USSN 14/198,992), 45 pages, Patent Interference No. 106,013, dated November 18, 2014 (Doc 133)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32694	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 2 (For Judgment Under 35 U.S.C. section 112(b)), 32 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 214)
13	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 2 (For Judgment Under 35 U.S.C. section 112(b)), 34 pages, Patent Interference No. 106,007, dated November 18, 2014 (Doc 211)
14	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Motion 3 (For judgment that Claims 11-12, 14-15, and 17-29 of Application No. 13/550,210 are barred under 35 U.S.C. section 135(b)), 25 Pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 215)
15	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Filing Priority Statement, 2 pages, Patent Interference No. 106,008, dated November 18, 2014 (Doc 218)
16	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Recent Authority, filed in Patent Interference No. 106,007, July 2, 2015, pages 1-16 (Doc 469).
17	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Recent Authority, filed in Patent Interference No. 106,007, September 2, 2015, pages 1-18 (Doc 470).
18	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Recent Authority, filed in Patent Interference No. 106,008, July 2, 2015, pages 1-16 (Doc 477)
19	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Recent Authority, filed in Patent Interference No. 106,008, September 2, 2015, pages 1-18 (Doc 478).
20	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Related Proceedings, Patent Interference No. 106,007, 3 pages, dated August 1, 2014 (Doc 11)
21	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Related Proceedings, Patent Interference No. 106,008, 5 pages, dated August 7, 2014 (Doc 11)
22	University of Western Australia v. Academisch Ziekenhuis Leiden, UWA Notice of Related Proceedings, Patent Interference No. 106,013, 3 pages, dated October 14, 2014 (Doc 6)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32695	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

23	US 7,960,541 (Wilton et al.), Pages 84, Exhibit Number 1002 filed in interferences 106,007 and 106,008 on November 18, 2014.
24	US 8,450,474 (Wilton et al.), Pages 95, Exhibit Number 1087 filed in interferences 106,007 and 106,008 on February 13, 2015.
25	US 8,455,634 (Wilton et al.) Pages 95, Exhibit Number 1088 filed in interferences 106,007 and 106,008 on February 13, 2015.
26	US 8,455,635 (Wilton et al.), Pages 96, Exhibit Number 1089 filed in interferences 106,007 and 106,008 on February 13, 2015.
27	US 8,455,636 (Wilton et al.), Pages 92, Exhibit Number 1003 filed in interferences 106,007 and 106,008 on November 18, 2014.
28	US 8,476,423 (Wilton et al.), Pages 95, Exhibit Number 1111 filed in interferences 106,007 and 106,008 on February 13, 2015.
29	US 8,501,703 (Bennett et al.), Pages 16, Exhibit Number 1090 filed in interferences 106,007 and 106,008 on February 13, 2015.
30	US 8,501,704 (Mourich et al.), Pages 39, Exhibit Number 1091 filed in interferences 106,007 and 106,008 on February 13, 2015.
31	US 8,524,676 (Stein et al.), Pages 28, Exhibit Number 1092 filed in interferences 106,007 and 106,008 on February 13, 2015.
32	US 8,524,880 (Wilton et al.), Pages 89, Exhibit Number 1093 filed in interferences 106,007 and 106,008 on February 13, 2015.
33	US 8,536,147 (Weller et al.), Pages 95, Exhibit Number 1094 filed in interferences 106,007 and 106,008 on February 17, 2015, Doc 251.



**INFORMATION DISCLOSURE  
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( Not for submission under 37 CFR 1.99)

Application Number # 32896	15705172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	US 8,592,386 (Mourich et al.), Pages 46, Exhibit Number 1095 filed in interferences 106,007 and 106,008 on February 13, 2015.
35	US 8,618,270 (Iversen et al.), Pages 28, Exhibit Number 1096 filed in interferences 106,007 and 106,008 on February 13, 2015.
36	US 8,637,483 (Wilton et al.), Pages 157, Exhibit Number 1097 filed in interferences 106,007 and 106,008 on February 13, 2015.
37	US 8,697,858 (Iversen), Pages 95, Exhibit Number 1098 filed in interferences 106,007 and 106,008 on February 13, 2015.
38	US 8,703,735 (Iversen et al.) Pages 73, Exhibit Number 1099 filed in interferences 106,007 and 106,008 on February 13, 2015.
39	US 8,741,863 (Moulton et al.), Pages 68, Exhibit Number 1100 filed in interferences 106,007 and 106,008 on February 13, 2015.
40	US 8,759,307 (Stein et al.), Pages 35, Exhibit Number 1101 filed in interferences 106,007 and 106,008 on February 13, 2015.
41	US 8,779,128 (Hanson et al.), Pages 104, Exhibit Number 1102 filed in interferences 106,007 and 106,008 on February 13, 2015.
42	US 8,785,407 (Stein et al.), Pages 35, Exhibit Number 1103 filed in interferences 106,007 and 106,008 on February 13, 2015.
43	US 8,785,410 (Iversen et al.), Pages 20, Exhibit Number 1104 filed in interferences 106,007 and 106,008 on February 13, 2015.
44	US 8,835,402 (Kole et al.), Pages 27, Exhibit Number 1105 filed in interferences 106,007 and 106,008 on February 13, 2015.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32697	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

45	US 8,865,883 (Sazani et al.), Pages 199, Exhibit Number 1106 filed in interferences 106,007 and 106,008 on February 13, 2015.
46	US 8,871,918 (Sazani et al.), Pages 195, Exhibit Number 1107 filed in interferences 106,007 and 106,008 on February 13, 2015.
47	US 8,877,725 (Iversen et al.), Pages 34, Exhibit Number 1108 filed in interferences 106,007 and 106,008 on February 13, 2015.
48	US 8,895,722 (Iversen et al.), Pages 29, Exhibit Number 1109 filed in interferences 106,007 and 106,008 on February 13, 2015.
49	US 8,906,872 (Iversen et al.), Pages 69, Exhibit Number 1110 filed in interferences 106,007 and 106,008 on February 13, 2015.
50	US Abandonment for Application No. 13/902,376, 1 page, dated June 12, 2014 (Exhibit Number 1047 filed in interferences 106008, 106007 on November 18, 2014)

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32698	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

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Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

**Electronic Acknowledgement Receipt**

<b>EFS ID:</b>	30440752
<b>Application Number:</b>	15705172
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	2879
<b>Title of Invention:</b>	ANTISENSE OLIGONUCLEOTIDES FOR INDUCING EXON SKIPPING AND METHODS OF USE THEREOF
<b>First Named Inventor/Applicant Name:</b>	Stephen Donald WILTON
<b>Customer Number:</b>	123147
<b>Filer:</b>	Amy E. Mandragouras/Anita Costa
<b>Filer Authorized By:</b>	Amy E. Mandragouras
<b>Attorney Docket Number:</b>	AVN-008CN41
<b>Receipt Date:</b>	22-SEP-2017
<b>Filing Date:</b>	
<b>Time Stamp:</b>	17:09:32
<b>Application Type:</b>	Utility under 35 USC 111(a)

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Submitted with Payment	no
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**File Listing:**

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1	Other Reference-Patent/App/Search documents	14857561.pdf	1608731 947b9988b72ea40658c310d99064672410c10ac0	no	32

**Warnings:**

Case 1:21-cv-01015-JLH Document 434-3 Filed 12/18/23 Page 207 of 224 PageID #: 32701					
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			83b83a17d90e75c623db608a4224a833f936ce90		
Warnings:					
Information:					
3	Other Reference-Patent/App/Search documents	14857590.pdf	724656	no	15
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Warnings:					
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4	Other Reference-Patent/App/Search documents	14858250.pdf	301186	no	8
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Warnings:					
Information:					
5	Other Reference-Patent/App/Search documents	14858416.pdf	630100	no	11
			edc9ef83ca7e3f120523aff0b698c8ee8f6c386f		
Warnings:					
Information:					
6	Other Reference-Patent/App/Search documents	14942629.pdf	301184	no	8
			5fc6031573de744eacde6224d885f73a3afb38d1		
Warnings:					
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7	Other Reference-Patent/App/Search documents	14944886.pdf	545217	no	10
			c3698910f183b78bb693d20e98307c17f23483f9		
Warnings:					
Information:					
8	Other Reference-Patent/App/Search documents	15274719.pdf	616134	no	13
			2a76889d8253f6f7c6b81f3d7a5f885dfc2ae07c		
Warnings:					
Information:					

9	Other Reference-Patent/App/Search documents	15274772.pdf	1091329  e58939198c3d325fa24a30570ef235c7985e ec3b	no	26
<b>Warnings:</b>					
<b>Information:</b>					
<b>Total Files Size (in bytes):</b>				6593782	
<p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>  <b>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</b></p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>  <b>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</b></p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>  <b>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</b></p>					



Doc code: IDS

# 32703

PTO/SB/08a (03-15)

Doc description: Information Disclosure Statement (IDS) Filed

Approved for use through 07/31/2016. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> ( Not for submission under 37 CFR 1.99)	Application Number	15705172
	Filing Date	2017-09-14
	First Named Inventor	Stephen Donald WILTON
	Art Unit	1674
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	AVN-008CN41

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32704	15705172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

1	US Amendment After Non-Final Action for Application No. 11/233,495, 31 pages, dated June 24, 2010 (Exhibit Number 2073 filed in interferences 106008, 106013, 106007 on November 18, 2014)
2	US Amendment for Application No. 11/233,495, 15 pages, dated April 1, 2009 (Exhibit Number 2071 filed in interferences 106008, 106013, 106007 on November 18, 2014)
3	US Amendment for Application No. 11/233,495, 19 pages, dated October 31, 2007 (Exhibit Number 2070 filed in interferences 106008, 106013, 106007 on November 18, 2014)
4	US Amendment for Application No. 11/233,495, 19 pages, dated September 16, 2009 (Exhibit Number 2072 filed in interferences 106008, 106013, 106007 on November 18, 2014)
5	US Amendment for Application No. 11/233,495, 9 pages, dated October 31, 2007 (Exhibit Number 2070 filed in interferences 106008, 106013, 106007 on November 18, 2014)
6	US Amendment for Application No. 11/570,691, 9 pages, dated June 15, 2010 (Exhibit Number 1043 filed in interferences 106008, 106007 on November 18, 2014)
7	US Amendment for Application No. 13/271,080, 30 pages, dated January 30, 2013 (Exhibit Number 1049 filed in interferences 106008, 106007 on November 18, 2014)
8	US Amendment for Application No. 13/902,376, 36 pages, dated March 21, 2014 (Exhibit Number 1046 filed in interferences 106008, 106007 on November 18, 2014)
9	US Amendment in Response to Advisory Action for Application No. 11/233,495, 23 pages, dated March 14, 2011 (Exhibit Number 2074 filed in interferences 106008, 106013, 106007 on November 18, 2014)
10	US Amendments to the Claims for Application No. 11/233,495, 4 pages, dated May 8, 2014 (Exhibit Number 2077 filed in interferences 106008, 106013, 106007 on November 18, 2014)
11	US Amendments to the Claims for Application No. 14/198,992, 3 pages, dated July 16, 2014 (Exhibit Number 2079 filed in interferences 106008, 106013, 106007 on November 18, 2014)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32705	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

12	US Applicant-Initiated Interview Summary and Notice of Allowance for Application No. 13/550,210, 9 pages dated May 19, 2014 (Exhibit Number 2076 filed in interferences 106008, 106013, 106007 on November 18, 2014)
13	US application as-filed and Preliminary Amendment for Application No. 13/550,210, 59 pages dated July 16, 2012 (Exhibit Number 2087 filed in interferences 106008, 106013, 106007 on November 18, 2014)
14	US Application as-filed for application No. 14/198,992, 52 pages, dated March 6, 2014 (Exhibit Number 2086 filed in interferences 106008, 106013, 106007 on November 18, 2014)
15	US Application as-filed, Application Data Sheet, and Preliminary Amendment for Application No. 12/837,359, 101 pages, dated July 15, 2010 (Exhibit Number 2100 filed in interferences 106008, 106013, 106007 on November 18, 2014)
16	US Application for Letters Patent for Application No. 11/233,495 as-filed and preliminary amendment, 77 pages, dated September 21, 2005 (Exhibit Number 2095 filed in interferences 106008, 106013, 106007 on November 18, 2014)
17	US Application No. 11/233,495, 74 pages; excerpts of prosecution history for including: US Supplemental Amendment and Response dated May 8, 2014; Second Supplemental Response dated July 5, 2013; Supplemental Amendment dated June 26, 2013; Amendment after Non-final Action dated November 1, 2010; Amendment under 35 USC 1.114 dated September 16, 2009 (Exhibit Number 2054 filed in interferences 106008, 106013, 106007 on November 18, 2014)
18	US Application No. 14/198,992, 17 pages; excerpts of prosecution history including: Supplemental Amendment dated July 16, 2014; Response to Non-Final Office Action dated July 14, 2014 (Exhibit Number 2056 filed in interferences 106008, 106013, 106007 on November 18, 2014)
19	US Application No. 14/248,279, 29 pages; excerpts of prosecution history including: Amendment under 37 CFR 1.312 dated September 19, 2014; Amendment in Response to Final Office Action dated August 7, 2014; Declaration under 37 CFR 1.132 dated May 26, 2014; Declaration under 37 CFR 1.132 dated May 27, 2014; Response dated June 3, 2014 (Exhibit Number 2057 filed in interferences 106008, 106013, 106007 on November 18, 2014)
20	US Application No. 13/550,210, 27 pages; excerpts of prosecution history including: Response and Amendment dated May 12, 2014; Response to Non-Final Office Action dated January 21, 2014; Second Preliminary Amendment dated January 3, 2013 (Exhibit Number 2055 filed in interferences 106008, 106013, 106007 on November 18, 2014)
21	US claim amendments for Application No. 13/550,210, 3 pages, dated May 12, 2014 (Exhibit Number 2078 filed in interferences 106008, 106013, 106007 on November 18, 2014)
22	US Claims for Application No. 12/976,381, 1 page, dated December 22, 2010 (Exhibit Number 2065 filed in interferences 106008, 106013, 106007 on November 18, 2014)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32706	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

23	US Declaration of Richard K. Bestwick, for Application No. 11/570,691, 5 pages, dated June 15, 2010 (Exhibit Number 1044 filed in interferences 106008, 106007 on November 18, 2014)
24	US E-mail from Patent Trial and Appeal Board to Danny Huntington, 2 pages, dated October 9, 2014 (Exhibit Number 2002 filed in interferences 106008 on October 17, 2014)
25	US Non-Final Office Action for Application No. 11/570,691, 16 pages, dated March 15, 2010 (Exhibit Number 1042 filed in interferences 106008, 106007 on November 18, 2014)
26	US Office Action for Application No. 13/271,080, 25 pages, dated July 30, 2012 (Exhibit Number 1048 filed in interferences 106008, 106007 on November 18, 2014)
27	US Office Action for Application No. 13/550,210, 12 pages, dated September 27, 2013 (Exhibit Number 2080 filed in interferences 106008, 106013, 106007 on November 18, 2014)
28	US Office Action for Application No. 13/902,376, 7 pages, dated January 7, 2014 (Exhibit Number 1045 filed in interferences 106008, 106007 on November 18, 2014)
29	US Patent Application No. 12/198,007 as-filed, 64 pages, dated August 25, 2008 (Exhibit Number 2092 filed in interferences 106008, 106013, and 106007 on November 18, 2014)
30	US Preliminary Amendment and application as-filed for Application No. 12/976,381, 64 pages, dated December 22, 2010 (Exhibit No. 2089 filed in Interferences 106007, 106008, and 106013 on November 18, 2014)
31	US Preliminary Amendment for Application No. 11/233,495, 10 pages, dated September 21, 2005 (Exhibit Number 2069 filed in interferences 106008, 106013, 106007 on November 18, 2014)
32	US Preliminary Remarks for Application No. 14/198,992, 1 page, dated March 6, 2014 (Exhibit Number 2097 filed in interferences 106008, 106013, 106007 on November 18, 2014)
33	US Proposed Terminal Disclaimer for Application No. 12/860,078, 2 pages, dated October 17, 2014 (Exhibit Number 2001 filed in interference 106008 on October 17, 2014)

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32707	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

34	US Remarks for Application No. 14/248,279, 2 pages, dated August 27, 2014 (Exhibit Number 2110 filed in interferences 106008, 106013, 106007 on November 18, 2014)
35	US Response and amendments for Application No. 13/550,210, 12 pages, dated January 21, 2014 (Exhibit Number 2063 filed in interferences 106008, 106013, 106007 on November 18, 2014)
36	US Revised Figure 4H, US Application No. 13/271,080, 1 page (Exhibit Number 1050 filed in interferences 106008, 106007 on November 18, 2014)
37	US Terminal Disclaimer for Application No. 14/198,992, 1 page, dated July 15, 2014 (Exhibit Number 2096 filed in interferences 106008, 106013, 106007 on November 18, 2014)
38	US Terminal Disclaimer for Application No. 14/248,279, 1 page, dated August 7, 2014 (Exhibit Number 2109 filed in interferences 106008, 106013, 106007 on November 18, 2014)
39	US Track One Request, Application as-filed, and Application Data Sheet for Application No. 14/248,279, 68 pages, dated April 8, 2014 (Exhibit Number 2108 filed in interferences 106008, 106013, 106007 on November 18, 2014)
40	US Transmittal, application as-filed, and Preliminary Amendment for Application No. 11/570,691, 102 pages, dated December 15, 2006 (Exhibit Number 2103 filed in interferences 106008, 106013, 106007 on November 18, 2014)
41	US Transmittal, application as-filed, and Preliminary Amendment for Application No. 13/270,992, 101 pages, dated October 11, 2011 (Exhibit Number 2098 filed in interferences 106008, 106013, 106007 on November 18, 2014)
42	US Transmittal, application as-filed, and Preliminary Amendment for Application No. 13/271,080, 115 pages, dated October 11, 2011 (Exhibit Number 2111 filed in interferences 106008, 106013, 106007 on November 18, 2014)
43	US Updated Filing Receipt for Application No. 13/550,210, 3 pages, dated December 11, 2012 (Exhibit Number 2044 filed in interferences 106008, 106013, 106007 on November 18, 2014)
44	USPTO "2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting or Involving...Natural Products" ("the March Guidance"), 19 pages, (Exhibit Number 2118 filed in interferences 106,007 and 106,008 on February 17, 2015.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32708	15705172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

45	USPTO Written Description Training Materials, Revised March 25, 2008, Example 12 (Exhibit Number 1068 filed in Interferences 106008, 106007 on December 23, 2014)
46	JWA Clean Copy of Claims and Sequence, as filed in Interference No. 106,007 on August 1, 2014 (Paper 12), 8 pages, (Exhibit Number 2126 filed in interferences 106,007 and 106,008 on February 17, 2015).
47	JWA Clean Copy of Claims and Sequence, as filed in Interference No. 106,007 on August 7, 2014 (Paper 12), 8 pages, (Exhibit Number 2127 filed in interferences 106,007 and 106,008 on February 17, 2015).
48	JWA Motion 1 (For Judgment Under 35 § 112(a)) from Int. No. 106,007 (PN 210), Pages 40, Exhibit Number 1005 filed in Interference 106,013 on February 17, 2015.
49	JWA Motion 1 (For Judgment Under 35 § 112(a)) from Int. No. 106,008 (Doc 213), Pages 38, Exhibit Number 1004 filed in Interference 106,013 on February 17, 2015.
50	JWA submission of teleconference transcript, 28 pages, dated December 12, 2014 (Exhibit Number 2114 filed in Interferences 106008 and 106007 on December 12, 2014)

If you wish to add additional non-patent literature document citation information please click the Add button

**EXAMINER SIGNATURE**

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

Application Number # 32709	15/05172
Filing Date	2017-09-14
First Named Inventor	Stephen Donald WILTON
Art Unit	1674
Examiner Name	Not Yet Assigned
Attorney Docket Number	AVN-008CN41

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Amy E. Mandragouras, Esq./	Date (YYYY-MM-DD)	2017-09-22
Name/Print	Amy E. Mandragouras, Esq.	Registration Number	36,207

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**



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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 22, 2017  
Electronic Signature for Amy E. Mandragouras, Esq.: /Amy E. Mandragouras, Esq./

Docket No.: AVN-008CN41  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Stephen Donald Wilton *et al.*

Application No.: 15/705,172

Confirmation No.: 2879

Filed: September 14, 2017

Art Unit: 1674

For: ANTISENSE OLIGONUCLEOTIDES FOR  
INDUCING EXON SKIPPING AND  
METHODS OF USE THEREOF

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In compliance with 37 C.F.R. § 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached PTO/SB/08. It is respectfully requested that the documents listed on the PTO/SB/08 be expressly considered by the Examiner during the prosecution of this application, and that the documents be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

For the Examiner's convenience in reviewing this continuation application, Applicant submits a consolidated PTO/SB/08, listing all references cited during the prosecution of the parent applications. The present application is a continuation of U.S. Application No. 15/274,772, filed September 23, 2016 (Atty. Docket No. AVN-008CN37). In accordance with 37 C.F.R. §1.98(d), copies of the references previously cited by or submitted to the Office in the parent applications are not enclosed, but will be provided upon request.

Application No.: 15/705,172 (Information Disclosure Statement)

Docket No.: AVN-008CN41

Applicant calls to the attention of the Examiner the following Applications and Office Actions issued therein:

<b>Applications</b>				
<i>Examiner's Initials</i>	<i>Serial No.</i>	<i>Filing Date</i>	<i>First Named Inventor</i>	<i>Docket No.</i>
	11/570,691	January 15, 2008	Stephen Donald Wilton	AVN-008
	12/837,356	July 15, 2010	Stephen Donald Wilton	AVN-008CN
	12/837,359	July 15, 2010	Stephen Donald Wilton	AVN-008CN2
	12/860,078	August 20, 2010	Stephen Donald Wilton	AVN-008CN3
	13/168,857	June 24, 2011	Stephen Donald Wilton	AVN-008CN4
	13/168,863	June 24, 2011	Stephen Donald Wilton	AVN-008CN5
	13/270,500	October 11, 2011	Stephen Donald Wilton	AVN-008CN6
	13/270,531	October 11, 2011	Stephen Donald Wilton	AVN-008CN7
	13/270,744	October 11, 2011	Stephen Donald Wilton	AVN-008CN8
	13/270,937	October 11, 2011	Stephen Donald Wilton	AVN-008CN9
	13/270,992	October 11, 2011	Stephen Donald Wilton	AVN-008CN10
	13/271,080	October 11, 2011	Stephen Donald Wilton	AVN-008CN11
	13/727,415	December 26, 2012	Stephen Donald Wilton	AVN-008CN12
	13/741,150	January 14, 2013	Stephen Donald Wilton	AVN-008CN13
	13/826,613	March 14, 2013	Stephen Donald Wilton	AVN-008CN14
	13/826,880	March 14, 2013	Stephen Donald Wilton	AVN-008CN15
	13/902,376	May 24, 2013	Stephen Donald Wilton	AVN-008CN17
	13/963,578	August 9, 2013	Stephen Donald Wilton	AVN-008CN18

Application No.: 15/705,172 (Information Disclosure Statement)

Docket No.: AVN-008CN41

	14/086,859	November 21, 2013	Stephen Donald Wilton	AVN-008CN19
	14/178,059	February 11, 2014	Stephen Donald Wilton	AVN-008CN20
	14/223,634	March 24, 2014	Stephen Donald Wilton	AVN-008CN22
	14/273,318	May 8, 2014	Stephen Donald Wilton	AVN-008CN23
	14/273,379	May 8, 2014	Stephen Donald Wilton	AVN-008CN24
	14/316,603	June 26, 2014	Stephen Donald Wilton	AVN-008CN25
	14/316,609	June 26, 2014	Stephen Donald Wilton	AVN-008CN26
	14/317,952	June 27, 2014	Stephen Donald Wilton	AVN-008CN27
	14/740,097	June 15, 2015	Stephen Donald Wilton	AVN-008CN28
	14/852,090	September 11, 2015	Stephen Donald Wilton	AVN-008CN29RCE
	14/852,149	September 11, 2015	Stephen Donald Wilton	AVN-008CN30
	14/857,555	September 17, 2015	Stephen Donald Wilton	AVN-008CN31
	14/857,561	September 17, 2015	Stephen Donald Wilton	AVN-008CN32RCE
	14/858,250	September 18, 2015	Stephen Donald Wilton	AVN-008CN33
	15/274,719	September 23, 2016	Stephen Donald Wilton	AVN-008CN36
	15/274,772	September 23, 2016	Stephen Donald Wilton	AVN-008CN37
	15/349,535	11-11-2016	Stephen Donald Wilton	AVN-008RE
	12/605,276	October 23, 2009	Peter SAZANI	AVN-009RCE
	13/829,545	March 14, 2013	Peter SAZANI	AVN-009CN
	13/830,253	March 14, 2013	Peter SAZANI	AVN-009CN2
	14/523,610	October 24, 2014	Peter SAZANI	AVN-009DV
	14/852,257	September 11, 2015	Peter SAZANI	AVN-009DVCN1RCE

Application No.: 15/705,172 (Information Disclosure Statement)

Docket No.: AVN-008CN41

	14/852,264	September 11, 2015	Peter SAZANI	AVN-009DVCN2
	14/857,569	September 17, 2015	Peter SAZANI	AVN-009DVCN3
	14/857,590	September 17, 2015	Peter SAZANI	AVN-009DVCN4
	14/858,416	September 18, 2015	Peter SAZANI	AVN-009DVCN5
	14/743,856	June 18, 2015	R.K. BESTWICK	AVN-10PCCN
	14/213,629	March 14, 2014	E.M. KAYE	AVN-012ARCE
	14/214,567	March 14, 2014	E.M. KAYE	AVN-012BRCE
	14/213,607	March 14, 2014	R.K. BESTWICK	AVN-013A
	14/214,480	March 14, 2014	R.K. BESTWICK	AVN-013BRCE
	14/942,629	November 16, 2015	R.K. BESTWICK	AVN-013ACN
	13/509,331	July 9, 2012	S.D. WILTON	AVN-015US
	14/108,137	December 16, 2013	S.D. WILTON	AVN-015USCN
	14/944,886	November 18, 2015	S.D. WILTON	AVN-015USCN2
	14/213,641	March 14, 2014	R.K. BESTWICK	AVN-017RCE
	14/776,533	September 14, 2015	R.K. BESTWICK	AVN-017CPUS

Office Actions (copies enclosed)			
<i>Examiner's Initials</i>	<i>Serial No.</i>	<i>Date Mailed from USPTO</i>	<i>Examiner</i>
	11/570,691	August 16, 2010	Kimberly Chong
	11/570,691	March 15, 2010	Kimberly Chong
	11/570,691	May 26, 2009	Kimberly Chong
	12/837,356	May 3, 2013	Kimberly Chong
	12/837,356	April 3, 2013	Kimberly Chong
	12/837,356	August 2, 2012	Kimberly Chong
	12/837,359	March 12, 2012	Kimberly Chong
	12/837,359	October 5, 2011	Kimberly Chong
	12/837,359	March 30, 2011	Kimberly Chong
	12/837,359	December 22, 2010	Kimberly Chong
	12/860,078	February 14, 2011	Kimberly Chong
	13/168,857	July 12, 2012	Kimberly Chong
	13/168,863	March 8, 2013	Kimberly Chong
	13/168,863	October 11, 2012	Kimberly Chong
	13/168,863	August 8, 2012	Kimberly Chong

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	13/270,500	March 15, 2013	Kimberly Chong
	13/270,500	July 30, 2012	Kimberly Chong
	13/270,500	March 14, 2012	Kimberly Chong
	13/270,531	June 28, 2012	Kimberly Chong
	13/270,531	March 14, 2012	Kimberly Chong
	13/270,744	April 3, 2013	Kimberly Chong
	13/270,744	August 6, 2012	Kimberly Chong
	13/270,744	March 14, 2012	Kimberly Chong
	13/270,937	February 25, 2013	Kimberly Chong
	13/270,937	June 14, 2012	Kimberly Chong
	13/270,937	March 14, 2012	Kimberly Chong
	13/270,992	April 4, 2013	Kimberly Chong
	13/270,992	July 30, 2012	Kimberly Chong
	13/270,992	March 16, 2012	Kimberly Chong
	13/271,080	March 26, 2013	Kimberly Chong
	13/271,080	July 30, 2012	Kimberly Chong
	13/271,080	March 14, 2012	Kimberly Chong
	13/727,415	February 6, 2013	Kimberly Chong
	13/741,150	March 16, 2015	Kimberly Chong
	13/741,150	September 18, 2014	Kimberly Chong
	13/741,150	April 11, 2014	Kimberly Chong
	13/741,150	September 24, 2013	Kimberly Chong
	13/826,613	July 22, 2014	Kimberly Chong
	13/826,613	January 7, 2014	Kimberly Chong
	13/826,613	July 17, 2013	Kimberly Chong
	13/826,880	June 22, 2015	Kimberly Chong
	13/826,880	January 26, 2015	Kimberly Chong
	13/826,880	April 15, 2014	Kimberly Chong
	13/826,880	September 11, 2013	Kimberly Chong
	13/902,376	June 5, 2014	Kimberly Chong
	13/902,376	January 7, 2014	Kimberly Chong
	13/902,376	July 18, 2013	Kimberly Chong
	13/963,578	September 24, 2013	Kimberly Chong
	14/086,859	June 30, 2014	Kimberly Chong
	14/086,859	January 27, 2014	Kimberly Chong
	14/178,059	March 31, 2014	Kimberly Chong
	14/223,634	April 15, 2015	Kimberly Chong
	14/273,318	October 20, 2014	Kimberly Chong
	14/273,318	July 3, 2014	Kimberly Chong
	14/273,379	July 7, 2014	Kimberly Chong
	14/316,603	March 10, 2015	Kimberly Chong
	14/316,603	September 26, 2014	Kimberly Chong

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	14/316,609	March 16, 2015	Kimberly Chong
	14/316,609	October 21, 2014	Kimberly Chong
	14/317,952	March 18, 2015	Kimberly Chong
	14/317,952	November 7, 2014	Kimberly Chong
	14/740,097	November 14, 2016	Kimberly Chong
	14/740,097	April 8, 2016	Kimberly Chong
	14/740,097	November 6, 2015	Kimberly Chong
	14/852,090	April 15, 2016	Kimberly Chong
	14/852,090	January 6, 2016	Kimberly Chong
	14/852,090	October 15, 2015	Kimberly Chong
	14/852,149	November 24, 2015	Kimberly Chong
	14/857,555	April 12, 2016	Kimberly Chong
	14/857,555	November 6, 2015	Kimberly Chong
	14/857,561	April 18, 2016	Kimberly Chong
	14/857,561	March 15, 2016	Kimberly Chong
	14/857,561	February 17, 2016	Kimberly Chong
	14/857,561	January 8, 2016	Kimberly Chong
	14/857,561	October 23, 2015	Kimberly Chong
	14/858,250	November 6, 2015	Kimberly Chong
	12/605,276	June 18, 2014	J. McDonald
	12/605,276	October 18, 2013	J. McDonald
	12/605,276	December 23, 2011	J. McDonald
	12/605,276	August 24, 2011	J. McDonald
	12/605,276	February 11, 2011	J. McDonald
	13/829,545	June 6, 2014	J. McDonald
	13/830,253	June 11, 2014	J. McDonald
	13/830,253	November 26, 2013	J. McDonald
	14/523,610	May 11, 2016	J. McDonald
	14/852,257	October 27, 2015	J. McDonald
	14/852,257	October 6, 2015	J. McDonald
	14/852,264	April 21, 2016	J. McDonald
	14/852,264	October 21, 2015	J. McDonald
	14/857,569	May 6, 2016	J. McDonald
	14/857,569	November 19, 2015	J. McDonald
	14/857,590	May 16, 2016	J. McDonald
	14/857,590	November 19, 2015	J. McDonald
	14/858,416	May 4, 2016	J. McDonald
	14/858,416	October 27, 2015	J. McDonald
	14/214,567	July 7, 2016	E. Poliakova-Georgan
	14/214,567	December 3, 2015	E. Poliakova-Georgan
	14/214,567	June 24, 2015	E. Poliakova-Georgan
	14/213,607	September 15, 2015	D.H. Shin



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	14/213,607	April 1, 2015	D.H. Shin
	14/213,607	September 18, 2014	D.H. Shin
	14/214,480	August 2, 2016	D.H. Shin
	14/214,480	October 19, 2015	D.H. Shin
	14/214,480	April 17, 2015	D.H. Shin
	14/214,480	September 19, 2014	D.H. Shin
	14/942,629	August 16, 2016	D.H. Shin
	13/509,331	September 16, 2013	T.A. Vivlemore
	13/509,331	January 28, 2013	T.A. Vivlemore
	14/108,137	April 29, 2015	T.A. Vivlemore
	14/108,137	October 9, 2015	T.A. Vivlemore
	14/108,137	October 3, 2014	T.A. Vivlemore
	14/944,886	April 27, 2017	T.A. Vivlemore
	14/944,886	September 30, 2016	T.A. Vivlemore
	14/213,641	August 1, 2016	D.H. Shin
	14/213,641	October 16, 2015	D.H. Shin
	14/213,641	March 31, 2015	D.H. Shin
	14/213,641	September 18, 2014	D.H. Shin
	14/213,629	May 23, 2016	E. Poliakova-Georgan
	14/213,629	August 21, 2015	E. Poliakova-Georgan
	14/213,629	December 29, 2014	E. Poliakova-Georgan
	14/743,856	August 1, 2016	A. Hudson Bowman
	14/776,533	February 28, 2017	D. Shin
	14/776,533	August 3, 2016	D. Shin
	15/274,719	December 16, 2016	K. Chong
	15/274,772	December 30, 2016	K. Chong
	15/274,772	September 18, 2017	K. Chong

The Examiner is requested to review the file histories of these applications, including cited references, Office Actions, Responses, etc., and is asked to contact Applicant's Attorney if the Examiner would like the Applicant to supply copies of any or all of the information included in any of these applications. For any of these applications, if Applicant's Attorney is not contacted by the Examiner with such a request, then it will be concluded that the Examiner has reviewed or will review the file content of these applications.

Applicant respectfully requests that the Examiner initial the blank columns next to the cited Applications and Office Actions, to indicate that the information has been considered by the Examiner. Alternatively, Applicant requests that the Examiner insert the phrase, "All references

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considered except where lined through,” on each page of the Information Disclosure Statement, along with the Examiner’s initials.

The filing of this Information Disclosure Statement is not to be interpreted as a representation that the cited documents are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any documents herein be construed *per se* as a representation that such document is prior art. Moreover, Applicant understands the Examiner will make an independent evaluation of the cited documents.

This Information Disclosure Statement is filed within three months of the U.S. filing date (37 C.F.R. § 1.97(b)(1)). Applicant believes no fee is due with this statement.

Dated: September 22, 2017

Respectfully submitted,

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